Psychosocial factors and physical inactivity in type 2 diabetes

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Psychosocial factors and physical inactivity in type 2 diabetes

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CHAPTER 1

General introduction

THE BURDEN OF TYPE 2 DIABETES AND ITS COMPLICATIONS

Currently, diabetes can be regarded as a global epidemic, affecting around 194 million people worldwide in 2003, a number which is expected to increase to 333 million people by 2025 (1). Additionally, for each diagnosed patient, another one is unaware of having diabetes. In the Netherlands, over 600.000 patients had diabetes in 2003 (2). Solely based on demographic data, the prevalence of diabetes is expected to increase by 32.5% between 2005 and 2025. However, this increase may even be more extensive, since prediction models do not account for the rising prevalence of overweight, which is an important contributor to type 2 diabetes (3), the most common type of diabetes. Type 2 diabetes affects generally older adults, but due to unfavorable lifestyle habits such as unhealthy diet and physical inactivity, the disease nowadays manifests itself at an increasing earlier age.

Type 2 diabetes is a chronic disease with a progressive nature, and is characterized by insulin resistance and/or abnormal insulin secretion, either of which may predominate (4). Type 2 diabetes is often part of a much broader underlying disorder, which is referred to as the metabolic syndrome. The metabolic syndrome is a cluster of risk factors for cardiovascular disease, including besides diabetes and its pre stage impaired glucose tolerance (IGT), hypertension, visceral obesity, dyslipidaemia, hyperinsulinaemia, hypercoagulability and microalbuminuria (4; 5). Subsequently, many macrovascular (e.g. coronary heart disease and stroke) and microvascular (e.g. retinopathy and nephropathy) conditions may occur in patients with type 2 diabetes (6). For example, having type 2 diabetes increases the risk of coronary heart disease 2-4 fold (7). On average, patients with type 2 diabetes lose 5-10 years of their lives, with cardiovascular disease being the major cause of death. The strong rise in the prevalence of type 2 diabetes will undoubtedly lead to increases in diabetes complications. The earlier onset of type 2 diabetes results in an increasing number of patients that has to cope with type 2 diabetes for a long part of their life, increasing the odds of developing complications. Consequently, the demands on health care capacity as well as the costs related to diabetes, which long term complications largely account for, will increase (8). More than ever, there is a need for effective treatment strategies in order to stem the burden of diabetes and its complications.

DIABETES MANAGEMENT

The main goal of diabetes management is the prevention or delay of vascular and neural complications (9). Diabetes management, which generally takes place in primary care, is complex and multifactorial, including oral medication/insulin therapy, self-control and making changes in health behaviors, such as diet and physical activity (10), and aimed at obtaining good glycemic control and management of cardiovascular risk factors. This implies that type 2 diabetes is basically a self-managed disease, demanding large responsibility of the patient for his/her own course of the disease (11). Dealing with this chronic and progressive disease, its multifactor treatment and the huge burden on self responsibility, is emotionally and behaviorally challenging, and has a great impact on the quality of life of the patient (12). The difficulty of attaining such a demanding regimen is reflected in the generally low adherence to medication regimens in type 2 diabetes patients, therewith reducing treatment effectiveness and increasing the incidence of complications (13). However, additionally to medical therapy, physical activity may be a powerful modality in the prevention of diabetes related complications.

PHYSICAL ACTIVITY

The following paragraphs address the aspects of physical (in)activity in relation to diabetes and factors that influence the level of physical activity.

Physical inactivity

In the last few decades, physical activity patterns of people in Western countries have thoroughly changed. Mechanization and automation have led to a situation in which physical activity is nowadays for a majority of people related to leisure time (e.g. sports and exercise) instead of integrated in daily routine. The simultaneously elevated food consumption makes that the human energy balance is disturbed. As a result physical inactivity and overweight are strongly increased, which in turn contributed to the increasing prevalence of type 2 diabetes (14). It is therefore not surprising that prevalence of physical inactivity in patients with type 2 diabetes is higher compared to the general population (14; 15).

Physical activity in diabetes management

Since physical inactivity is an important contributing factor to type 2 diabetes, physical activity seems a logical prevention modality to use in counteracting further progression of the disease. A large body of research has shown numerous positive effects of physical activity on type 2 diabetes (16; 17). Physical activity can be defined as 'bodily movement produced by

contraction of skeletal muscle that requires energy expenditure in excess of resting expenditure' (16). A subset of physical activity is exercise, which can be defined as 'planned, structured, and repetitive bodily movement performed to improve or maintain one or more components of physical fitness' (16). Traditionally, efficacy of physical activity in patients with type 2 diabetes has been studied in structured exercise interventions. Positive effects were shown on glycemic control, independent of weight loss (17; 18), as well as on insulin sensitivity (14; 16). Furthermore, studies in the general population (19), as well as in patients with type 2 diabetes showed several cardioprotective benefits of exercise, e.g. improvement of blood pressure, lipid profile, and long-term weight management (14; 16). However, probably the most important benefit of physical activity in type 2 diabetes is the improvement of cardiorespiratory fitness (VO_2-max) (19), which is conversely related with mortality and therefore an effective means in the prevention and delay of complications (19). Besides, physical activity may not only have a protective effect on diabetes related complications, but on the development of co morbidities as well, which have also shown to contribute to the burden of illness, by impairing physical function (20). However, despite the great potential of physical activity, few people with type 2 diabetes seem to profit. A gap is to be bridged when translating research findings into clinical practice. Currently, physical activity is undervalued and underused in diabetes practice, and physical inactivity in patients with type 2 diabetes is high (21; 22). Furthermore, long term adherence to exercise interventions is frequently low (14). Therefore, it may be useful to identify factors related to physical activity in the first place.

Factors related to physical activity

Physical activity is a complex and dynamic health behavior (23). A large body of research is available about factors related to physical activity in the general population. These include demographic, biological, psychological, behavioral, social, and environmental factors (23; 24). The strongest and most consistent associations are found between physical activity and demographic factors. Physically active people are more likely to be male, younger, and higher educated (24). Little is known about factors related to physical activity and their relative contribution in type 2 diabetes, and results are inconsistent (18-25). Since type 2 diabetes generally affects elderly people, age may be an important factor. Another correlate of physical inactivity associated with type 2 diabetes is overweight/obesity (23; 24). Furthermore, impaired physical ability induced by aging, complications and co morbidities, may be a significant barrier to physical activity in this population (25). However, psychosocial factors may also play and important role in physical activity in patients with type 2 diabetes.

PSYCHOSOCIAL FACTORS

Psychosocial problems have a large contribution in the burden of illness (26), and largely affect quality of life (12). The psychosocial impact of diabetes has been referred to as a more important determinant of mortality in patients with diabetes than many other clinical and physiological factors (12). Two psychosocial factors, which have both shown to be associated with cardiovascular disease will be studied in this thesis, namely depression and Type D personality.

Depression

Depression is worldwide one of the leading contributors to the burden of disease, and is an important cause of disability (27). It is a common mental disorder that presents with symptoms as depressed mood, loss of interest or pleasure, feelings of guilt or low self-esteem, low energy, poor concentration, apathetic or agitated behavior, disturbed sleep or appetite, and thoughts about death and suicide, which may, when they endure or become recurrent, lead to impaired ability of the individual to manage daily responsibilities. Regarding the definition and prevalence of depression, a distinction has to be made between depressive syndrome (major depression), and depressive symptoms (sub-threshold depression). At least one of the two core symptoms (depressed mood and loss of interest), as well as four other symptoms as described above, have to be present for at least two weeks to meet the DSM-IV criteria for diagnosis of depressive syndrome (28). Individuals with sub-threshold depression do experience symptoms of depression, but do not meet the DSM-IV criteria for major depression (29). Prevalence of major depression is 1-3% in people over 50 years of age, while clinically relevant symptoms of depression are present in 8-16% of this population (30; 31). Individuals with sub-threshold depression experience substantial impairment of psychosocial functioning and well-being (30), and depressive symptoms may lead to impairment in health status as well as functional status with a nearly similar degree as major depression (32). Prevalence of depression is generally higher in women, individuals without a partner, and the low educated (33). Furthermore, it has been shown that depression is more common in people who have a chronic disease (34). In the present thesis, the term 'depression' indicates occurrence of depressive symptoms.

Although prevalence of depression is high in patients with type 2 diabetes (17.6%), and more common than in those without diabetes (9.8%) (35), it is under recognized in treatment (36; 37), especially in elderly people, which are generally represented in the diabetes population (38). Furthermore, few of the diagnosed patients are actually treated for depression (36; 39). Prevalence of depressive symptoms has shown to be associated with disability (40), impaired quality of life (41) and mortality (42) in patients with

diabetes. Additionally, depression is often associated with unhealthy lifestyle (43). The reasons for the increased prevalence of depression and type 2 diabetes are not fully understood, but the presence of complications may in particular play a role. For example, a meta-analysis on the relationship between depressive symptoms and diabetes complications showed a significant relationship between depressive symptoms and the number as well as the severity of several diabetes complications such as neuropathy, macrovascular complications (e.g. coronary heart disease), and retinopathy (44).

Type D personality

Another psychological factor that is mentioned in relation to health and disease is personality (45; 46). Personality refers to a complex organization of traits that reflect consistencies in the general affective level and behavior of patients (47). It is proposed that personality may affect health by three possible mechanisms, namely by influencing physiological reactions associated with health; by affecting adjustment to health conditions, and by affecting health behavior practices (48).

A relatively new personality trait studied in relation to cardiovascular disease is the so called distressed or Type D personality, which represents the synergy of negative affectivity and social inhibition (49). The negative affectivity trait implicates the tendency to experience negative emotions across time and situations, including dysphoria and feelings of tension and worry (47). However, additionally to experiencing these negative emotions, Type D individuals tend to inhibit expression of emotions and behaviors in social interactions to avoid disapproval (social inhibition trait) (50). It is the paradoxical combination of both traits that may have important implications for treatment and clinical outcomes (51). Patients with a Type D personality have a predisposition to chronic distress. This indicates that some Type D individuals will experience severe distress reaching diagnostic thresholds of psychopathologic disorders, while others may reach this point only under stressful conditions, and again others may even never experience pathological levels of distress. Type D personality has been associated with a wide range of adverse health outcomes, such as increased risk of morbidity and mortality, but also the risk for clustering psychological factors such as depression and anxiety (49). The underlying mechanisms of the link between Type D personality and cardiovascular disease are not fully understood. As indicated above, Type D personality may affect health outcomes either directly by influencing physiological reactions, and/or indirectly by psychosocial mechanisms. One of these psychosocial mechanisms may be unhealthy behaviors, such as smoking, physical inactivity and poor diet, which Type D individuals may be more likely to engage in. Another may be related to the low social support these individuals may often perceive (52).

Little research has been performed on the association of personality traits and health outcomes in patients with diabetes (53). Currently, Type D personality has not been studied yet in patients with type 2 diabetes. However, this may be interesting since type 2 diabetes is considered a risk factor for cardiovascular disease.

Psychosocial factors in diabetes management

Psychosocial problems may negatively influence the course of disease. Both depression (54) and Type D personality (55) may lead to poor treatment adherence, self-management activities, and lifestyle behaviors which diabetes management basically relies on. Prevalence of depressive symptoms has been shown to negatively interfere with glycemic control (56), although others did not find this association (57; 58). Psychosocial factors may thus partly explain the large variability in response to treatment modalities such as medication, diet, and physical activity, as seen within diabetes populations (53).

ASSOCIATIONS BETWEEN PSYCHOSOCIAL FACTORS AND PHYSICAL ACTIVITY

Several studies in the general population have shown that depressed people are less likely to engage in physical activities (59; 60), and less likely to adhere to physical activity intervention (61). Being depressed may negatively influence readiness to change (37), and hence hamper the adoption to a physically active lifestyle. Personality has increasingly gained interest in health and exercise psychology (45). It is hypothesized that personality affects social cognitions (e.g. perceptions, attitudes, outcome expectations, self-efficacy) towards a specific health behavior, e.g. physical activity, and thereby influencing the health behavior itself (48). Rhodes and Smith (2006), conducted a meta-analysis on the relationship between personality and physical activity. They reported extraversion and conscientiousness to be positive correlates, while neuroticism was shown to be a negative correlate of physical activity (45). Individuals high on neuroticism, which is closely related to the negative affectivity component of Type D personality, are more likely to experience negative emotions, distress, and depression, which may negatively affect participation in physical activity (45). Furthermore, Kircaldy et al. (2002) showed that socially inhibited individuals were less likely to engage in physical activity (62). In the context of type 2 diabetes, the knowledge about the role of psychosocial factors in physical activity is scarce.

Conversely, physical activity had also been shown to have positive effects on psychosocial factors in the general population. Physical activity has shown to be a stress reducing factor (14), and is positively associated with health related quality of life (63; 64). Furthermore, several epidemiological studies

showed a positive effect of physical activity on depression (65). Harris et al. (2006), performed a study in which they followed a cohort of depressed adults during 10 years (59). They concluded that higher levels of physical activity were associated with less concurrent depression, and additionally physical activity buffered the negative effects of experiencing medical conditions. The strength of physical activity, in comparison with drug therapy, may therefore lie in multiple physiological and psychosocial benefits.

RATIONALE, SETTING AND DESIGN OF THE THESIS

Rationale of the thesis

The large expected increase of the prevalence of type 2 diabetes and its complications in the next 25 years calls for effective diabetes management. Therefore, it is most relevant to study factors influencing outcomes and effectiveness of diabetes care (66). Physical activity may be an important additional modality to prevent or delay complications. Given the high prevalence of physical inactivity and poor adherence to physical activity in patients with type 2 diabetes, an understanding of the factors restraining regular engagement in physical activity is warranted. However, little is known about the factors related to physical inactivity in patients with type 2 diabetes, and especially information about the role of psychosocial factors is scarce. Knowledge of the factors related to physical inactivity may eventually lead to identifying patients at risk as well as provide key factors for intervention, which are both important in successfully and systematically promoting physical activity in diabetes care.

Design and setting of the thesis: The DIAZOB project

The data used in this thesis were collected within the diabetes management project 'DIAZOB' (Diabetes Care Zuid-Oost Brabant), which includes a cohort of 3300 patients with type 2 diabetes recruited from 100 general practitioners in the Eindhoven region, the Netherlands, and was assembled in 2005. In the 'DIAZOB' project, patients will be followed during their lifetime and are periodically assessed for biological parameters and demographic, psychosocial, and lifestyle parameters by patient survey with a one year interval. Furthermore, processes of care are registered in order to assess quality of care provided. The studies in this thesis include cross-sectional data of the baseline assessments. Currently, in the year 2008, about 10.000 patients with type 2 diabetes from 140 general practitioners are included in the DIAZOB project, and two yearly follow-up assessments have been performed.

AIM AND OUTLINE OF THE THESIS

The aim of this thesis is to study possible factors related to physical inactivity in patients with type 2 diabetes, with an emphasis on psychosocial factors.

Five research questions have been formulated:

1 What is the efficacy of structured exercise interventions in patients with type 2 diabetes according to current literature?

2 Is vascular co-morbidity related to depression in patients with type 2 diabetes, and which other factors are related to depression in this population?

3 Is depression associated with physical inactivity in patients with type 2 diabetes?

4 What is the prevalence of Type D personality in patients with type 2 diabetes?

5 Is Type D personality associated with physical inactivity in patients with type 2 diabetes?

The general outline of the thesis is as follows: Chapter 2 consists of a systematic review of structured group exercise interventions in type 2 diabetes. In a meta-analysis, the effect size of exercise intervention on HbA_{1c} and cardiovascular risk factors is determined. Chapter 3 describes the prevalence of depression in insulin naïve patients with type 2 diabetes, thereby controlling for vascular co-morbidities and other potential confounders. Chapter 4 encloses a study of the association between depression and physical inactivity in type 2 diabetes patients. In chapter 5, the prevalence of Type D personality is examined in type 2 diabetes patients. Furthermore, this chapter outlines the association between Type D personality and physical inactivity, as well as the association between Type D personality and depression. In addition, chapter 6 presents the combined effects of having a Type D personality and being without a partner on physical inactivity and depression, separately. Finally, main outcomes, strengths and weaknesses of the studies are discussed in chapter 7. Recommendations for future research as well as for clinical practice are provided.

REFERENCES

1. Diabetes Atlas, third edition. International Diabetes Federation, 2006
2. Poortvliet MC, Schrijvers CTM, Baan CA: Diabetes in Nederland. Bilthoven, RIVM, 2007
3. Baan CA, Rijken PM: Volksgezondheid Toekomstverkenning, Nationaal Kompas Volksgezondheid. Bilthoven, RIVM, 2005
4. Zimmet P, Alberti KG, Shaw J: Global and societal implications of the diabetes epidemic. Nature 414:782-787, 2001
5. Reynolds K, He J: Epidemiology of the metabolic syndrome. Am J Med Sci 330:273-279, 2005
6. McKinlay J, Marceau L: US public health and the 21st century: diabetes mellitus. Lancet 356:757-761, 2000
7. Adler AI: Managing diabetes: what to do about cardiovascular disease. Diabetes Res Clin Pract 61 Suppl 1:S3-8, 2003
8. Boutayeb A, Twizell EH, Achouayb K, Chetouani A: A mathematical model for the burden of diabetes and its complications. Biomed Eng Online 3:20, 2004
9. Rutten GEHM, De Grauw WJC, Uitewaal PJM, Van der Does FEE, Heine RJ, Van Ballegooie E, Verduijn MM, Bouma M: NHG-Standaard Diabetes mellitus type 2. Huisarts Wet 49:137-152, 2006
10. Standards of medical care in diabetes--2006. Diabetes Care 29 Suppl 1:S4-42, 2006
11. Snoek F, Visser A: Improving quality of life in diabetes: how effective is education? Patient Educ Couns 51:1-3, 2003
12. Delamater AM, Jacobson AM, Anderson B, Cox D, Fisher L, Lustman P, Rubin R, Wysocki T: Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. Diabetes Care 24:1286-1292, 2001
13. Vermeire E, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A: Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. Cochrane Database Syst Rev:CD003638, 2005
14. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
15. Welschen LM, van Oppen P, Dekker JM, Bouter LM, Stalman WA, Nijpels G: The effectiveness of adding cognitive behavioural therapy aimed at changing lifestyle to managed diabetes care for patients with type 2 diabetes: design of a randomised controlled trial. BMC Public Health 7:74, 2007
16. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C: Physical activity/exercise and type 2 diabetes. Diabetes Care 27:2518-2539, 2004
17. Thomas D, Elliott E, Naughton G: Exercise for type 2 diabetes mellitus. Cochrane Database Syst Rev 3:CD002968, 2006

18. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ: Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. Jama 286:1218-1227, 2001
19. Boule NG, Kenny GP, Haddad E, Wells GA, Sigal RJ: Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. Diabetologia 46:1071-1081, 2003
20. Plotnikoff RC, Lippke S, Karunamuni N, Eves N, Courneya KS, Sigal R, Birkett NJ: Co-morbidity, functionality and time since diagnosis as predictors of physical activity in individuals with type 1 or type 2 diabetes. Diabetes Res Clin Pract 78:115-122, 2007
21. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW: Are health care professionals advising patients with diabetes or at risk for developing diabetes to exercise more? Diabetes Care 29:543-548, 2006
22. Poskiparta M, Kasila K, Kiuru P: Dietary and physical activity counselling on type 2 diabetes and impaired glucose tolerance by physicians and nurses in primary healthcare in Finland. Scand J Prim Health Care 24:206-210, 2006
23. Sherwood NE, Jeffery RW: The behavioral determinants of exercise: implications for physical activity interventions. Annu Rev Nutr 20:21-44, 2000
24. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W: Correlates of adults' participation in physical activity: review and update. Med Sci Sports Exerc 34:1996-2001, 2002
25. Kaplan MS, Newsom JT, McFarland BH, Lu L: Demographic and psychosocial correlates of physical activity in late life. Am J Prev Med 21:306-312, 2001
26. Barry LC, Lichtman JH, Spertus JA, Rumsfeld JS, Vaccarino V, Jones PG, Plomondon ME, Parashar S, Krumholz HM: Patient satisfaction with treatment after acute myocardial infarction: role of psychosocial factors. Psychosom Med 69:115-123, 2007
27. Michaud CM, Murray CJ, Bloom BR: Burden of disease--implications for future research. Jama 285:535-539, 2001
28. Association AP: Diagnostic an Statistical Manual of Mental Disorders. Washington, DC, American Psychiatric Association, 1994
29. Cuijpers P, Smit F: Subthreshold depression as a risk indicator for major depressive disorder: a systematic review of prospective studies. Acta Psychiatr Scand 109:325-331, 2004
30. Beekman AT, Deeg DJ, van Tilburg T, Smit JH, Hooijer C, van Tilburg W: Major and minor depression in later life: a study of prevalence and risk factors. J Affect Disord 36:65-75, 1995
31. Cole MG, Dendukuri N: Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. Am J Psychiatry 160:1147-1156, 2003

32. Wagner HR, Burns BJ, Broadhead WE, Yarnall KS, Sigmon A, Gaynes BN: Minor depression in family practice: functional morbidity, co-morbidity, service utilization and outcomes. Psychol Med 30:1377-1390, 2000
33. Pouwer F, Beekman AT, Nijpels G, Dekker JM, Snoek FJ, Kostense PJ, Heine RJ, Deeg DJ: Rates and risks for co-morbid depression in patients with Type 2 diabetes mellitus: results from a community-based study. Diabetologia 46:892-898, 2003
34. Fenton WS, Stover ES: Mood disorders: cardiovascular and diabetes comorbidity. Curr Opin Psychiatry 19:421-427, 2006
35. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K: The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med 23:1165-1173, 2006
36. Piette JD, Richardson C, Valenstein M: Addressing the needs of patients with multiple chronic illnesses: the case of diabetes and depression. Am J Manag Care 10:152-162, 2004
37. Pouwer F, Beekman AT, Lubach C, Snoek FJ: Nurses' recognition and registration of depression, anxiety and diabetes-specific emotional problems in outpatients with diabetes mellitus. Patient Educ Couns 60:235-240, 2006
38. Volkers AC, Nuyen J, Verhaak PF, Schellevis FG: The problem of diagnosing major depression in elderly primary care patients. J Affect Disord 82:259-263, 2004
39. Jack L, Jr., Airhihenbuwa CO, Namageyo-Funa A, Owens MD, Vinicor F: The psychosocial aspects of diabetes care. Using collaborative care to manage older adults with diabetes. Geriatrics 59:26-31; quiz 32, 2004
40. Von Korff M, Katon W, Lin EH, Simon G, Ludman E, Oliver M, Ciechanowski P, Rutter C, Bush T: Potentially modifiable factors associated with disability among people with diabetes. Psychosom Med 67:233-240, 2005
41. Eren I, Erdi O, Sahin M: The effect of depression on quality of life of patients with type II diabetes mellitus. Depress Anxiety, 2007
42. Katon WJ, Rutter C, Simon G, Lin EH, Ludman E, Ciechanowski P, Kinder L, Young B, Von Korff M: The association of comorbid depression with mortality in patients with type 2 diabetes. Diabetes Care 28:2668-2672, 2005
43. Bonnet F, Irving K, Terra JL, Nony P, Berthezene F, Moulin P: Depressive symptoms are associated with unhealthy lifestyles in hypertensive patients with the metabolic syndrome. J Hypertens 23:611-617, 2005
44. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ: Association of depression and diabetes complications: a meta-analysis. Psychosom Med 63:619-630, 2001

45. Rhodes RE, Smith NE: Personality correlates of physical activity: a review and meta-analysis. Br J Sports Med 40:958-965, 2006
46. Wasserman LI, Trifonova EA: Diabetes mellitus as a model of psychosomatic and somatopsychic interrelationships. Span J Psychol 9:75-85, 2006
47. Watson D, Clark LA, Harkness AR: Structures of personality and their relevance to psychopathology. J Abnorm Psychol 103:18-31, 1994
48. Rhodes RE: The built-in environment: the role of personality and physical activity. Exerc Sport Sci Rev 34:83-88, 2006
49. Denollet J: DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med 67:89-97, 2005
50. Asendorpf JB: Social inhibition: a general– developmental perspective. In Emotion, Inhibition, and Health Traue HC, Pennebaker JW, Eds. Seattle, Hogrefe & Huber Publishers, 1993, p. 80-99
51. Kupper N, Denollet J, de Geus EJ, Boomsma DI, Willemsen G: Heritability of type-D personality. Psychosom Med 69:675-681, 2007
52. Williams L, O'Connor RC, Howard S, Hughes BM, Johnston DW, Hay JL, O'Connor DB, Lewis CA, Ferguson E, Sheehy N, Grealy MA, O'Carroll RE: Type-D personality mechanisms of effect: the role of health-related behavior and social support. J Psychosom Res 64:63-69, 2008
53. Lane JD, McCaskill CC, Williams PG, Parekh PI, Feinglos MN, Surwit RS: Personality correlates of glycemic control in type 2 diabetes. Diabetes Care 23:1321-1325, 2000
54. Katon WJ: Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biol Psychiatry 54:216-226, 2003
55. Schiffer AA, Denollet J, Widdershoven JW, Hendriks EH, Smith OR: Failure to consult for symptoms of heart failure in patients with a type-D personality. Heart 93:814-818, 2007
56. Lustman PJ, Clouse RE: Depression in diabetic patients: the relationship between mood and glycemic control. J Diabetes Complications 19:113-122, 2005
57. Georgiades A, Zucker N, Friedman KE, Mosunic CJ, Applegate K, Lane JD, Feinglos MN, Surwit RS: Changes in depressive symptoms and glycemic control in diabetes mellitus. Psychosom Med 69:235-241, 2007
58. Knol MJ, Heerdink ER, Egberts AC, Geerlings MI, Gorter KJ, Numans ME, Grobbee DE, Klungel OH, Burger H: Depressive symptoms in subjects with diagnosed and undiagnosed type 2 diabetes. Psychosom Med 69:300-305, 2007
59. Harris AH, Cronkite R, Moos R: Physical activity, exercise coping, and depression in a 10-year cohort study of depressed patients. J Affect Disord 93:79-85, 2006
60. Hong S, Bardwell WA, Natarajan L, Flatt SW, Rock CL, Newman VA, Madlensky L, Mills PJ, Dimsdale JE, Thomson CA, Hajek RA, Chilton JA,

Pierce JP: Correlates of physical activity level in breast cancer survivors participating in the Women's Healthy Eating and Living (WHEL) Study. Breast Cancer Res Treat 101:225-232, 2007
61. Wing RR, Phelan S, Tate D: The role of adherence in mediating the relationship between depression and health outcomes. J Psychosom Res 53:877-881, 2002
62. Kirkcaldy BD, Shephard RJ, Siefen RG: The relationship between physical activity and self-image and problem behaviour among adolescents. Soc Psychiatry Psychiatr Epidemiol 37:544-550, 2002
63. Bize R, Johnson JA, Plotnikoff RC: Physical activity level and health-related quality of life in the general adult population: A systematic review. Prev Med 45:401-415, 2007
64. Rejeski WJ, Mihalko SL: Physical activity and quality of life in older adults. J Gerontol A Biol Sci Med Sci 56 Spec No 2:23-35, 2001
65. Stathopoulou G, Powers MB, Berry AC, Smits JAJ, Otto MW: Exercise Interventions for Mental Health: A Quantitative and Qualitative Review. Clin Psychol Sci Prac 13 179-193, 2006
66. van Dam HA, van der Horst FG, Knoops L, Ryckman RM, Crebolder HF, van den Borne BH: Social support in diabetes: a systematic review of controlled intervention studies. Patient Educ Couns 59:1-12, 2005

CHAPTER 2:

The effects of aerobic training, resistance training, or both, in the management of type 2 diabetes: a meta-analysis of randomized-controlled trials

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Submitted for publication

ABSTRACT

Background: Recently, accent in physical activity research in type 2 diabetes shifted from aerobic exercise to resistance training interventions or a combination of both. The aim of this study was to conduct a meta-analysis of randomized controlled trials in order to assess the effects of these interventions in the management of type 2 diabetes.

Methods: Trials were identified through searches of electronic bibliographic databases supplemented with hand searches of retrieved references. Included studies were randomized controlled trials, and compared structured exercise interventions with non-exercise control groups. Weighted mean differences were used to determine the effects of exercise versus non-exercise per exercise mode.

Results: Eighteen eligible trials were identified. Exercise resulted in a significant reduction of 0.63 (aerobic training), 0.38 (resistance training), and 0.77 (combined training) percentage points HbA_{1c}, respectively. Furthermore, combined training significantly improved HDL cholesterol levels (+ 0.13 mmol/l). Systolic blood pressure (-6.92 mmHg), as well as diastolic blood pressure (-4.91 mmHg) were significantly lowered after combined training, and VO_2-max also showed significant improvement (+ 3.37 ml min^{-1} kg^{-1}), however after correction for heterogeneity these effects did not remain significant any more.

Conclusions: The meta-analysis showed a significant reduction of HbA_{1c} induced by all three exercise modes.

INTRODUCTION

Currently, diabetes can be regarded as a global epidemic, affecting around 194 million people worldwide in 2003, a number which is expected to increase to 333 million people by 2025 when accounting for demographic changes alone (1). Development of type 2 diabetes is not only due to changes in demographic variables (mainly aging), but is also caused by overweight and physical inactivity, nowadays two emerging epidemics (2). The increase in prevalence of type 2 diabetes, therefore, tends to be much stronger.

Type 2 diabetes is a complex disease, characterized by a disturbance in glucose and fat metabolism, and high co-morbidity. Uncontrolled disease may lead to vascular and neural complications in the long-term and type 2 diabetes increases the risk of coronary heart disease 2-4 fold (3).

Disease control is highly influenced by lifestyle habits, emphasizing great responsibility of the patient for his own course of disease. Treatment, therefore, largely depends on the self-management capabilities of the patient (4). However, treatment adherence is low in this population (5). The slow progressive nature of the disease in which the patient often experiences no physical complaints, makes it difficult to understand the seriousness of the disease, until insulin treatment becomes necessary and/or complications appear.

Disease management has largely focused on disease control by medication and diet with little attention to the benefits of physical activity. However, several epidemiological studies have shown benefits of physical activity on glycemic control (6-9), insulin sensitivity (6; 8; 9), cardiovascular risk factors (6), cardiorespiratory fitness (10), and weight management in type 2 diabetes (6; 8; 9). Besides, due to its strong negative association with morbidity and mortality, physical activity is a powerful means to delay or prevent complications.

Despite the significance of physical activity in treatment and management of type 2 diabetes, it is underused in routine diabetes care consultations (11). Since physical inactivity is highly prevalent in individuals with type 2 diabetes, and they often have a history of inactivity, maximum exercise capacity (VO_2-max) in individuals with type 2 diabetes is on average lower than in healthy persons (12). Patients are often not familiar with the positive effects of physical activity or have negative experiences or associations with it. Furthermore, (severe) overweight is common in this population, which is a barrier to being physically active.

Traditionally, most exercise intervention studies in type 2 diabetes populations have incorporated structured, supervised aerobic exercise. Aerobic training programs involve repetitive large muscle group exercises and are aimed at improving cardiorespiratory fitness. Muscle mass is the largest and most important site of glucose storage. Increasing muscle mass therefore may have a great potential to affect glycemic control and insulin

resistance, especially in older adults in whom muscle mass has decreased. Resistance training as a specific mode to accomplish this, therefore, recently gained interest (13). Thus, both aerobic training and resistance training may be beneficial in type 2 diabetes, however in different ways. A combination of these two modalities seems to be a promising strategy in managing type 2 diabetes. The objective of this study is to conduct a meta-analysis of randomized controlled trials in order to assess the effects of aerobic training, resistance training, or a combination of both, in the management of type 2 diabetes.

METHODS

Data sources

Studies for this meta-analysis were obtained from searches of the following electronic bibliographic databases: The Cochrane Library, MEDLINE and EMBASE. The databases were searched from January 1986 up and until November 2007 and supplemented with hand searches of references of review articles and potentially eligible studies. Language was not restricted. Search terms regarding type 2 diabetes were adapted from the Cochrane Metabolic and Endocrine Disorders Group. Other key words used in the computerized literature searches were: physical activity, exercise, training, aerobic exercise, aerobic training, resistance exercise, resistance training, strength exercise, strength training, weight lifting, walking, circuit weight training.

Study selection

The selection of studies, and data abstraction was conducted by two authors (BK and VP), independent of each other. Disagreements were resolved by consensus. An exercise intervention was defined as a pre-determined program including specific recommendations for the type, frequency, duration and intensity of physical activity with a specific objective (14). The inclusion criteria applied in this meta-analysis were as follows: (1) randomized controlled trials (RCTs) comparing exercise versus non-exercise control, exercise plus diet versus diet alone or exercise plus medication versus medication alone, (2) prescribed aerobic training, resistance training or a combination of both for at least eight weeks, (3) adult males and females classified as having type 2 diabetes by study authors, (4) assessment of at least HbA_{1c} as an outcome measure. Physical activity counseling studies, and studies in which patients were recommended to increase their physical activities to a certain level were excluded, since in these studies it is difficult to document the actual training volume and intensity.

Data abstraction

Data extracted from each study included variables of the following categories: (1) study characteristics (randomization method, allocation concealment, blinding of outcome assessors, intention-to-treat analysis); (2) sample characteristics (inclusion and exclusion criteria, total number of participants in the intervention and control group, sex, age, duration of diabetes, baseline characteristics, diagnostic criteria, similarity of groups at baseline, dropout and compliance): (3) intervention and control characteristics (intervention duration, and type, frequency, duration, and intensity of the training program), (4) primary outcome (HbA_{1c}), and (5) secondary outcomes, and (6) results (means and standard deviations or 95% confidence interval of baseline and post-intervention continuous variables and possible adverse advents).

Statistical analysis

The primary outcome measure was long-term glycemic control, indicated by HbA_{1c} (%). Additional outcome measures were body mass (kg), BMI (kg/m^2), cardiorespiratory fitness expressed as VO_2-max ($ml\ min^{-1}\ kg^{-1}$), lipid profile (total cholesterol, low-density lipoprotein-cholesterol (LDL), high- density lipoprotein-cholesterol (HDL), triglycerides) (mmol/l), and blood pressure (mmHg). Although morbidity/complications and total mortality are important outcomes in diabetes intervention research, the timeframe of the exercise interventions (generally short-term) is not appropriate to investigate these outcomes.

Analyses were performed in Review Manager 4.2. Net changes in the primary and secondary outcomes were calculated as the difference (exercise minus control) of the post-intervention mean outcome values. Pooled effects were calculated for each exercise mode separately, by assigning weights equal to the inverse of the standard error for net changes in all outcomes. In case no post-intervention measures of dispersion were provided, the standard deviation of the baseline mean was used. All analyses were performed with a fixed effects model.

Heterogeneity between the outcomes of the studies was tested using the I^2 parameter of inconsistency, which is defined as $I^2 = 100\% * (Q-df)/Q$ (Q: chi-squared statistic, df: degrees of freedom). When inconsistency was greater than 50%, the studies were considered as heterogeneous. In that case, we excluded each study from the analyses once in order to detect the potential source of heterogeneity.

Methodological quality (internal validity) of the randomized clinical trials was scored on the Delphi list (15). The Delphi list is a valid and reliable 9 item checklist concerning patient selection, outcome measurement, and statistical analysis (16). The number of positively scored validity items yields a sum score. Blinding of participants and providers of the intervention could not be applied, so only the blinding of the outcome assessors was assessed. Scores therefore ranged from 0 to 7. The cut-off point was set at 50% and therefore high quality studies were defined by a score of 4 and higher and studies of poor quality by a score of 3 and less (17).

RESULTS

Of the 27 potentially appropriate randomized controlled studies retrieved, eighteen studies were included, as summarized in table 1 (18-35). One author was contacted for missing post intervention outcomes of the control group, which were rapidly provided (31). Nine randomized controlled trial were excluded for the following reasons: involving home-based training in a study sample that already received a structured exercise intervention (36); providing flexibility training (37), relaxation (38), or education (39) to the control group, which was not provided to the intervention group; comparing two exercise interventions (40); providing co-intervention in the intervention group which was not provided to the control group (41); not providing post-intervention results of the control group (42); also including participants with impaired glucose tolerance (43); and applying a trial duration of less than eight weeks (44). Cuff et al. (18), and Sigal et al. (24) compared two, respectively three different exercise modes to a non-exercise control group. For both studies, all intervention groups are included in the meta-analysis and compared separately to their control group. Wing et al. performed two comparisons of which only the comparison of exercise plus diet versus diet only is incorporated in this meta-analysis (26).

The eighteen included studies consisted of nine aerobic training (AT) interventions (18-26), five resistance training (RT) interventions (24; 27-30), and seven interventions combining aerobic and resistance training (AT+RT) (18; 24; 31-35). Characteristics of the included studies are shown in table 1. In total, 917 participants were included of which 541 were allocated to an exercise intervention (AT: 187, RT: 138, AT+RT: 216, respectively).

Furthermore, up to ten outcomes were available for pooling. Sample size varied from 16 to 251 participants. Percentage male participants ranged from 0% to 100%. Mean age of the samples ranged from 45 to 67 years, mean duration of diabetes ranged from 2 to 10 years, and mean HbA_{1c} at baseline ranged from 6.9 to 11.7%. Five studies had an intervention duration of less than three months (21; 26; 27; 29; 34), and eight studies had a duration of three to six months (18; 19; 22-25; 28; 32; 35). Three studies applied a duration of six months (20; 24; 30) and two studies lasted one year (31; 33).

Only six studies were of high quality (see table 1) (18; 19; 24; 27; 28; 34). Although all described as randomized controlled trials, only Dela et al. and Sigal et al. reported the method of randomization used (19; 24). Allocation concealment of treatment was only reported by Sigal et al. (24). Participants in the intervention group of Balducci et al. were significantly younger and had significantly lower blood pressure than participants in the control group (31). In the study of Castaneda et al., a significantly higher proportion of subjects on insulin therapy was found in the control group at baseline. However, data analysis showed that insulin use did not affect the training effect (28). Blinding of the outcome assessor was only described by Sigal et al., and Castaneda et al. (except for assessment of muscle strength) (24; 28). Drop-out rates were acceptable and ranged from 0 to 28%, with an average drop-out rate of 10% (AT), 12% (RT), and 7% (AT+RT), respectively, in the intervention groups, and 8% in the control groups. Five studies had no dropouts (18; 19; 26; 27; 34).

Table 1: Characteristics of included studies

Author	Subjects n (I/C)	% male	Length	Exercise target	Outcomes	Quality of study
Aerobic training						
Cuff et al. (2003) (A) (18)*	18 (9/9)	0	16 wk	3x/wk 75 min. aerobic exercise at 60-75% HRR	HbA_{1c}, body mass, VO_2-peak, lipid profile	4
Dela et al. (2004) (19)	16 (9/7)	100	3 mo	5x/wk 20 min. aerobic exercise at 75% VO_2-max	HbA_{1c}, body mass, BMI	5
Middlebrooke et al. (2006) (20)	59 (29/30)	54	6 mo	3x/wk 30 min. aerobic exercises at 70-80% HR-max	HbA_{1c}, body mass, BMI, VO_2-max, lipid profile, blood pressure	3
Mourier et al. (1997) (21)	24 (12/12)	83	10 wk	3x/wk 35-55 min. aerobic exercise at 50-85% VO_2-peak	HbA_{1c}, body mass, BMI, VO_2-max, lipid profile	3
Raz et al. (1994) (22)	40 (20/20)	35	12 wk	3x/wk 50 min. aerobic exercise of moderate intensity	HbA_{1c}, BMI, lipid profile	3
Ronnemaa et al. (1986) (23)	30 (15/15)	33	4 mo	5-7x/wk 45 min. aerobic exercise at 70% VO_2-max	HbA_{1c}, body mass, VO_2-max, lipid profile	3
Sigal et al. (2007) (A) (24)**	123 (60/63)	65	6 mo	3x/wk 45 min. aerobic exercise at 75% HR-max	HbA_{1c}, body mass, BMI, lipid profile, blood pressure	7
Tsujiuchi et al. (2002) (25)	36 (18/18)	-	4 mo	1x/wk 120 min. Qi-gong of low intensity	HbA_{1c}, BMI	2
Wing et al. (1988) (26)	30 (15/15)	30	10 wk	4x/wk 60 min. aerobic exercise of moderate intensity	HbA_{1c}, body mass, BMI, lipid profile, blood pressure	3

Table 1: continued

Author	Subjects n (I/C)	% male	Length	Exercise target	Outcomes	Quality of study
Resistance training						
Baldi et al. (2003) (27)	18 (9/9)	100	10 wk	3x/wk 2 sets (1st week 1 set) 12 rep. whole body exercise at 10-RM (upper body) and 15 RM (lower body) moderate intensity	HbA_{1c}, body mass, lipid profile	4
Castaneda et al. (2002) (28)	62 (31/31)	36	16 wk	3x/wk 45 min., intensity: wk 1-8: 60-80%, wk 10-14: 70-80% 1-RM	HbA_{1c}, body mass, lipid profile, blood pressure	5
Dunstan et al. (1998) (29)	27 (15/12)	63	8 wk	3x/wk 60 min. 3 sets, 10-15 rep. circuit weight training at 50-55% 1 RM (first 6 sessions 2 sets)	HbA_{1c}, body mass, BMI, blood pressure	3
Dunstan et al. (2002) (30)	36 (19/17)	55	6 mo	3x/wk 45 min. 3 sets, 8-10 rep. whole body exercise at 75-80% 1-RM (50-60% 1-RM in first 2 wks)	HbA_{1c}, body mass, lipid profile, blood pressure	3
Sigal et al. (2007) (B) (24)**	127 (64/63)	64	6 mo	3x/wk, 2-3 sets, 7-9 rep. whole body exercise at 7-9RM	HbA_{1c}, body mass, BMI, lipid profile, blood pressure	7

*I, intervention group; C, control group; HR-max, maximal heart rate; BMI, body mass index; VO_2-max / VO_2-peak, maximal/peak oxygen capacity; RM, repetition maximum; AT, aerobic training; HRR, heart rate reserve. * Cuff et al. included two intervention groups: aerobic training (A), and aerobic+ resistance training (B). Both groups are separately included in the analyses and compared with the control group.** Sigal et al. included three intervention groups: aerobic training (A), resistance training (B), and aerobic + resistance training (C). All three groups are separately included in the analyses and compared with the control group.*

Table 1: continued

Author	Subjects n (I/C)	% male	Length	Exercise target	Outcomes	Quality of study
Aerobic + resistance training						
Balducci et al. (2004) (31)	120 (62/58)	50	1 yr	3x/wk 30 min. of AT at 40–80% HRR and 30 min RT at 40-60% 1-RM	HbA_{1c}, BMI, lipid profile, blood pressure	2
Bjørgaas et al. (2005) (32)	29 (15/14)	100	12 wk	2x/wk 45 min. jogging, co-ordination exercise, knee bends, stretching at 50-85% HR-max, and 15 min. resistance exercises	HbA_{1c}, body mass, VO_2-max, lipid profile, blood pressure	3
Cuff et al. (2003) (B) (18)*	19 (10/9)	0	16 wk	3x/wk 75 min. aerobic exercise at 60-75% HRR and 2 sets 12 rep. 5 resistance exercises for lower extremity and trunk, low initial intensity, progressed as technique permitted	HbA_{1c}, body mass, VO_2-peak, lipid profile	4
Loimaala et al. (2003) (33)	50 (25/25)	100	1 yr	4x/wk (2x aerobic (1 unsupervised) + 2x resistance training) at least 30 min. walking at 65-75% VO_2-max and 3 sets 10-12 rep. of whole body exercise at 70-80% 1-RM	HbA_{1c}, BMI, VO_2-max, blood pressure	3

Table 1: continued

Author	Subjects n (I/C)	% male	Length	Exercise target	Outcomes	Quality of study
Aerobic + resistance training						
Maiorana et al. (2002) (34)	16 (cross over)	88	8 wk	3x/wk 1h. whole body exercise (cycle ergometry, treadmill walking, whole body resistance exercise) at 85% HR-peak and 65% 1-RM (circuit training)	HbA_{1c}, body mass, VO_2-peak, lipid profile	4
Sigal et al. (2007) (C) (24)**	127 (64/63)	64	6 mo	3x/wk 45 min. aerobic exercise at 75% HR-max, and 2-3 sets, 7-9 rep. whole body exercise at 7-9RM	HbA_{1c}, body mass, BMI, lipid profile, blood pressure	7
Tessier et al. (2001) (35)	45 (24/21)	59	16 wk	3x/wk 1 h. 20 min. walking at 60-79% VO_2-max, and 20 min. 2 sets, 20 rep. whole body exercise at low intensity (elastic bands)	HbA_{1c}, body mass, BMI	3

*I, intervention group; C, control group; HR-max, maximal heart rate; BMI, body mass index; VO_2-max / VO_2-peak, maximal/peak oxygen capacity; RM, repetition maximum; AT, aerobic training; HRR, heart rate reserve. * Cuff et al. included two intervention groups: aerobic training (A), and aerobic+ resistance training (B). Both groups are separately included in the analyses and compared with the control group.** Sigal et al. included three intervention groups: aerobic training (A), resistance training (B), and aerobic + resistance training (C). All three groups are separately included in the analyses and compared with the control group.*

Table 2, shows that compared to non-exercise control, exercise resulted in a significant reduction of 0.63 (aerobic training), 0.38 (resistance training), and 0.77 (combined aerobic and resistance training) percentage points HbA_{1c}, respectively.

Furthermore, table 3 shows a small, but significant, effects of combined aerobic and resistance training on systolic blood pressure, as well as diastolic blood pressure. However, heterogeneity was found between the outcomes of systolic (I^2 = 70.0%) and diastolic (I^2 = 56.1%) blood pressure of the combined aerobic and resistance training interventions. When the study of Balducci et al. (31) was excluded, inconsistency dropped to 19.6% (systolic blood pressure), and 0% (diastolic blood pressure), respectively. The overall effects of AT+RT on systolic blood pressure (WMD -1.70 mmHg, 95% CI [-7.19, 3.80]), and diastolic blood pressure (WMD -1.06 mmHg, 95% CI [-5.43, 3.32]), were no longer significant after exclusion of this study (p = 0.54, and p = 0.64, respectively).

Cardiorespiratory fitness, measured by VO_2-max/VO_2-peak (ml min^{-1} kg^{-1}) was reported in six studies (18; 20-23; 32; 34). Bjørgaas et al. reported data of VO_2-max as median and range, Cuff et al. reported data as (l/min.) and these studies were therefore excluded from analysis. Aerobic exercise had a significant effect on cardio respiratory fitness. However, again, considerable heterogeneity was found in the four studies that measured VO_2-max (I^2 = 75.5%), mostly attributable to the study of Mourier et al. (21). By excluding this study, the effect of exercise on VO_2-max was no longer significant (WMD 1.80 ml min^{-1} kg^{-1}, 95% CI [-0.18, 3.78], p = 0.08).

Exercise intervention did not elicit any changes in body mass, nor in BMI. No significant effects of exercise on lipid profile was obtained, except for the effect of combined aerobic and resistance training on HDL cholesterol. Finally, heterogeneity was found in the results of the resistance training studies for the outcomes of systolic blood pressure (I^2 = 59.6%), and HDL cholesterol (I^2 = 75.5%). After exclusion of the study of Castaneda et al. (28), and Dunstan et al. (30), respectively, inconsistency dropped to zero, but both effects remained non significant (p = 0.90, and p = 0.56).

Table 2: Weighted mean differences of the primary outcome, per exercise mode

Outcome	N participants (analyzed)	WMD [95% CI]
HbA_{1c} (%)	n (I/C)	
Aerobic training	*333*	*-0.63 [-0.91, -0.35]**
Cuff, 2003 (A)	18 (9/9)	-0.07 [-0.86, 0.27]
Dela, 2004	16 (9/7)	-0.30 [-1.96, 1.36]
Middlebrooke, 2006	52 (22/30)	-0.30 [-0.86, 0.26]
Mourier, 1997	22 (10/11)	-1.50 [-2.38, -0.62]
Raz, 1994	38 (19/19)	-1.20 [-3.42, 1.02]
Ronnemaa, 1986	25 (13/12)	-1.30 [-2.71, 0.11]
Sigal, 2007 (A)	108 (49/59)	-0.62 [-1.18, -0.06]
Tsujiuchi, 2002	26 (16/10)	-0.84 [-1.81, 0.13]
Wing, 1988	28 (13/15)	-0.80 [-1.63, 0.03]
Resistance training	*245*	*-0.38 [-0.74, -0.02]**
Baldi, 2003	18 (9/9)	0.00 [-1.66, 1.66]
Castaneda, 2002	62 (31/31)	-0.70 [-1.40, 0.00]
Dunstan, 1998	21 (11/10)	-0.30 [-1.98, 1.38]
Dunstan, 2002	29 (16/13)	-0.20 [-0.97, 0.57]
Sigal, 2007 (B)	115 (56/59)	-0.33 [-0.88, 0.22]
Aerobic + resistance training	*393*	*-0.77 [-1.05, -0.49]**
Balducci, 2004	112 (57/55)	-1.21 [-1.73, -0.69]
Bjørgaas, 2005	25 (14/11)	-0.22 [-1.17, 0.73]
Cuff, 2003 (B)	19 (10/9)	-0.07 [-1.18, 1.04]
Loimaala, 2003	49 (24/25)	-0.70 [-1.48, 0.08]
Maiorana, 2002	32 (16/16)	-0.60 [-1.58, 0.38]
Sigal, 2007 (C)	117 (58/59)	-0.95 [-1.50, -0.40]
Tessier, 2000	39 (19/20)	-0.20 [-1.05, 0.65]

I, intervention group; C, control group

** significant effect ($p < 0.05$)*

Table 3: Weighted mean differences of the secondary outcomes, per exercise mode

Outcome	N participants (analyzed)	WMD [95% CI]
Blood pressure		
Systolic blood pressure (mmHg)		
Aerobic training	188 (3 studies) (20; 24; 26)	-0.46 [-6.36, 5.44]
Resistance training	227 (4 studies) (24; 28-30)	-3.76 [-8.60, 1.09]
Aerobic + resistance training	393 (4 studies) (24; 31-33)	-6.92 [-10.95, -2.89]**
Diastolic blood pressure (mmHg)		
Aerobic training	188 (3 studies) (20; 24; 26)	0.07 [-3.41, 3.55]
Resistance training	227 (4 studies) (24; 28-30)	-0.81 [-3.15, 1.54]
Aerobic + resistance training	247 (3 studies) (24; 31; 32)	-4.91 [-6.80, -3.02]**
Cardio respiratory fitness		
VO_2-max (ml min^{-1} kg-1)	147 (4 studies) (20; 21; 23; 33)	3.37 [1.60, 5.13]**
Body composition		
Body mass (kg)		
Aerobic training	269 (7 studies) (18-21; 23; 24; 26)	-0.04 [-4.69, 4.62]
Resistance training	245 (5 studies) (24; 27-30)	-0.42 [-4.94, 4.11]
Aerobic + resistance training	230 (5 studies) (18; 24; 32; 34; 35)	-1.39 [-6.24, 3.46]
Body mass index		
Aerobic training	235 (5 studies) (19-22; 24)	0.78 [-0.65, 1.21]
Resistance training	136 (2 studies) (24; 29)	-1.87 [-3.96, 0.21]
Aerobic + resistance training	317 (4 studies) (24; 31; 33; 35)	-0.96 [-2.16, 0.23]

** significant effect ($p < 0.05$)*

*** significant effect, but after correcting for heterogeneity no longer significant*

Table 3: continued

Outcome	N participants (analyzed)	WMD [95% CI]
Lipid profile		
Total cholesterol (mmol/l)		
Aerobic training	159 (5 studies) (20-23; 26)	-0.02 [-0.31,0.27]
Resistance training	91 (2 studies) (28; 30)	0.03 [-0.37, 0.43]
Aerobic + resistance training	169 (3 studies) (31; 32; 34)	-0.12 [-0.46, 0.21]
LDL cholesterol (mmol/l)		
Aerobic training	201 (4 studies) (20; 21; 23; 24)	0.22 [-0.31,0.27]
Resistance training	206 (3 studies) (24; 28; 30)	-0.16 [-0.43, 0.12]
Aerobic + resistance training	261 (3 studies) (24; 31; 34)	0.04 [-0.28, 0.36]
HDL cholesterol (mmol/l)		
Aerobic training	267 (6 studies) (20-24; 26)	0.02 [-0.09, 0.05]
Resistance training	206 (3 studies) (24; 28; 30)	-0.03 [-0.13, 0.07]
Aerobic + resistance training	286 (4 studies) (24; 31; 32; 34)	0.13 [0.02, 0.23]*
Triglycerides (mmol/l)		
Aerobic training	267 (6 studies) (20-24; 26)	-0.10 [-0.35, 0.15]
Resistance training	144 (2 studies) (24; 30)	-0.20 [-0.60, 0.20]
Aerobic + resistance training	286 (4 studies) (24; 31; 32; 34)	-0.31 [-0.68, 0.05]

** significant effect (p < 0.05)*

*** significant effect, but after correcting for heterogeneity no longer significant*

DISCUSSION

This review of eighteen exercise interventions (n = 844, analyzed) showed a significant decrease in levels of HbA_{1c} after aerobic training, resistance training, or both, with the largest effect obtained after a combination of aerobic and resistance training. The effects on HbA_{1c} found in this study were independent of weight loss, and are comparable to those shown in two previous meta-analysis (7; 45). Subgroup effects for exercise mode found in the current meta-analysis were slightly lower for all three exercise modes (aerobic training: WMD -0.63 versus –0.70, resistance training: WMD –0.38 versus –0.5, combined training: WMD -0.77 versus –0.80), compared to the results of the meta-analysis of Snowling et al. (46).

The effects of combined exercise on blood pressure were significant, but heterogeneous. Thomas et al., found no significant effects of exercise on blood pressure, whereas Snowling et al., reported small to moderate effects after aerobic training and combined training, but not after resistance training (45; 46). Exercise also had a positive effect on VO_2-max, but this effect was lower than the overall effects found in the meta-analyses of Boulé et al. (10) and Thomas et al. (45). Furthermore, exercise intervention did not produce significant differences in lipid profile, except for a significant improvement of HDL-cholesterol level after combined aerobic and resistance training, which was similar to the results of Snowling et al. (46). Kelley et al. (47), found only a significant effect of aerobic exercise on LDL-cholesterol, whereas Thomas et al. only found significant improvements in triglyceride levels (45).

Although the effects of structured exercise training on type 2 diabetes seem to be modest, they are of clinical significance for cardiovascular risk reduction. Recently, in the UK Prospective Diabetes Study (UKPDS)75, the relative importance of glucose and blood pressure control in Type 2 diabetes was assessed (48). Observational data of 3,418 patients showed an additive risk reduction of 21% per 1 percentage point HbA_{1c} decrease, and 11% per 10 mmHg reduction in systolic blood pressure for any diabetes-related end point. For comparison, HbA_{1c} level decreased with 0.63-0.77 percentage points in the AT and AT+RT trials, and systolic blood pressure in the current meta-analysis decreased about 7 mmHg after combined aerobic and resistance training.

Furthermore, risk reduction can also be achieved by improvement of cardiorespiratory fitness (10). Low cardiorespiratory fitness and inactivity, both highly prevalent in the diabetes population, have been indicated as independent predictors of all-cause mortality in individuals with diabetes (10). Blair et al. found that an increase of 1.44 ml min^{-1} kg^{-1} in VO_2-max equals a 7.9% reduction in overall mortality (49). The increase of 1.80 ml min^{-1} kg^{-1} in VO_2-max found in this meta-analysis after correction for heterogeneity is slightly higher. Gregg et al. showed that a low intensive activity such as walking for at least two hours per week was associated with a significant reduction in all cause (39%) and cardiovascular mortality rate (34%) in adults with diabetes (50). Interestingly, there also seems to be no clear dose response relationship between exercise intensity and lowering of HbA_{1c} (45; 46), and blood pressure (51).

When interpreting findings from the studies included in this meta-analysis several methodological issues need to be mentioned. Only six studies (all published after 2001) applied an intention-to-treat analysis (18; 19; 24; 27; 28; 34). Not performing an intention-to-treat analysis may overestimate intervention effectiveness (52). Furthermore, the studies included showed mixed results within the three different exercise modes, which makes it difficult to document the real effect of exercise on type 2 diabetes. This variability may exist because of differences in trial length, intervention

characteristics (e.g. exercise intensity), and subject characteristics (e.g. baseline HbA_{1c} values). One of the strongest limitations of the studies included in this review is the low power due to small sample size. Only Sigal et al. reported a sample size calculation (24), and only three studies reached an adequate statistical power (21; 24; 31). Moreover, the interventions included in this meta-analysis are of relatively short duration lacking information about long-term adherence. Two studies applied a follow-up period up to 12 months post-intervention (22; 26). Both showed some beneficial effect in participants who continued exercising, however losses of follow-up were high. Participants in the study of Dunstan et al. continued exercising in a home-based resistance training program of six months (36). Improvement of glycemic control could not be maintained despite improvements in muscle strength and lean body mass, which was probably due to the decreased exercise intensity obtained in the home-based program and lower adherence to the exercise regimen. Another issue is the generalizability of the results: it might be questioned whether positive results obtained in a small, often highly selected, relatively well-controlled, motivated group under optimal conditions, may guarantee the effectiveness of the exercise intervention at population level.

The above mentioned previous meta-analyses apply different inclusion criteria (e.g. controlled clinical trials versus randomized controlled trials only, inclusion of studies providing co-intervention), different statistical analyses, and include different numbers of studies, which may lead to differences in findings. The strength of the current meta-analysis lies in the relative high number of participants available for pooling, which increases statistical power, and which made it possible to assess the effects of physical training per exercise modality. Furthermore, contrary to some meta-analyses (7; 46) the current meta-analysis included randomized trials only, which may less bias the results.

Although, a combination of aerobic and resistance training elicited somewhat lager benefits than the two exercise modes separately, it is based on the current meta-analysis not possible to make a clear statement of which exercise mode is the best for individuals with type 2 diabetes. To study whether exercise interventions will work at population level more research is needed on the effects of exercise interventions in long-term (>1 year), with special attention to the possibility of making the intervention easily available for large groups of individuals, in real world settings. Furthermore, the use of other outcomes is required, such as adherence, quality of life, adverse events, and morbidity. Study effects should be analyzed on an intention-to-treat basis, in order to obtain information about the effectiveness of exercise in the management of type 2 diabetes. Finally, larger study samples are needed to obtain sufficient power to determine the effects of the different exercise modalities on type 2 diabetes.

REFERENCES

1. Diabetes Atlas, third edition. International Diabetes Federation, 2006
2. Fletcher B, Gulanick M, Lamendola C: Risk factors for type 2 diabetes mellitus. J Cardiovasc Nurs 16:17-23, 2002
3. Adler AI: Managing diabetes: what to do about cardiovascular disease. Diabetes Res Clin Pract 61 Suppl 1:S3-8, 2003
4. Snoek FJ: Breaking the barriers to optimal glycaemic control--what physicians need to know from patients' perspectives. Int J Clin Pract Suppl:80-84, 2002
5. Vermeire E, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A: Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. Cochrane Database Syst Rev:CD003638, 2005
6. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
7. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ: Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. Jama 286:1218-1227, 2001
8. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C: Physical activity/exercise and type 2 diabetes. Diabetes Care 27:2518-2539, 2004
9. Tudor-Locke CE, Bell RC, Meyers AM: Revisiting the role of physical activity and exercise in the treatment of type 2 diabetes. Can J Appl Physiol 25:466-492, 2000
10. Boule NG, Kenny GP, Haddad E, Wells GA, Sigal RJ: Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. Diabetologia 46:1071-1081, 2003
11. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW: Are health care professionals advising patients with diabetes or at risk for developing diabetes to exercise more? Diabetes Care 29:543-548, 2006
12. Regensteiner JG, Sippel J, McFarling ET, Wolfel EE, Hiatt WR: Effects of non-insulin-dependent diabetes on oxygen consumption during treadmill exercise. Med Sci Sports Exerc 27:875-881, 1995
13. Willey KA, Singh MA: Battling insulin resistance in elderly obese people with type 2 diabetes: bring on the heavy weights. Diabetes Care 26:1580-1588, 2003
14. Bouchard C, Shephard R, Stephens T: Physical activity, fitness, and health: international proceedings and consensus statement, Champaign, Ill, Human Kinetics Publishers, 1994
15. Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Bouter LM, Knipschild PG: The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J Clin Epidemiol 51:1235-1241, 1998

16. Verhagen AP, de Vet HC, de Bie RA, Boers M, van den Brandt PA: The art of quality assessment of RCTs included in systematic reviews. J Clin Epidemiol 54:651-654, 2001
17. Verhagen AP, de Bie RA, Lenssen AF, de Vet HC, Kessels AG, Boers M, van den Brandt PA: Impact of quality items on study outcome. Treatments in acute lateral ankle sprains. Int J Technol Assess Health Care 16:1136-1146, 2000
18. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ: Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. Diabetes Care 26:2977-2982, 2003
19. Dela F, von Linstow ME, Mikines KJ, Galbo H: Physical training may enhance beta-cell function in type 2 diabetes. Am J Physiol Endocrinol Metab 287:E1024-1031, 2004
20. Middlebrooke AR, Elston LM, Macleod KM, Mawson DM, Ball CI, Shore AC, Tooke JE: Six months of aerobic exercise does not improve microvascular function in type 2 diabetes mellitus. Diabetologia 49:2263-2271, 2006
21. Mourier A, Gautier JF, De Kerviler E, Bigard AX, Villette JM, Garnier JP, Duvallet A, Guezennec CY, Cathelineau G: Mobilization of visceral adipose tissue related to the improvement in insulin sensitivity in response to physical training in NIDDM. Effects of branched-chain amino acid supplements. Diabetes Care 20:385-391, 1997
22. Raz I, Hauser E, Bursztyn M: Moderate exercise improves glucose metabolism in uncontrolled elderly patients with non-insulin-dependent diabetes mellitus. Isr J Med Sci 30:766-770, 1994
23. Ronnemaa T, Mattila K, Lehtonen A, Kallio V: A controlled randomized study on the effect of long-term physical exercise on the metabolic control in type 2 diabetic patients. Acta Med Scand 220:219-224, 1986
24. Sigal RJ, Kenny GP, Boule NG, Wells GA, Prud'homme D, Fortier M, Reid RD, Tulloch H, Coyle D, Phillips P, Jennings A, Jaffey J: Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med 147:357-369, 2007
25. Tsujiuchi T, Kumano H, Yoshiuchi K, He D, Tsujiuchi Y, Kuboki T, Suematsu H, Hirao K: The effect of Qi-gong relaxation exercise on the control of type 2 diabetes mellitus: a randomized controlled trial. Diabetes Care 25:241-242, 2002
26. Wing RR, Epstein LH, Paternostro-Bayles M, Kriska A, Nowalk MP, Gooding W: Exercise in a behavioural weight control programme for obese patients with Type 2 (non-insulin-dependent) diabetes. Diabetologia 31:902-909, 1988
27. Baldi JC, Snowling N: Resistance training improves glycaemic control in obese type 2 diabetic men. Int J Sports Med 24:419-423, 2003

28. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, Roubenoff R, Tucker KL, Nelson ME: A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. Diabetes Care 25:2335-2341, 2002
29. Dunstan DW, Puddey IB, Beilin LJ, Burke V, Morton AR, Stanton KG: Effects of a short-term circuit weight training program on glycaemic control in NIDDM. Diabetes Res Clin Pract 40:53-61, 1998
30. Dunstan DW, Daly RM, Owen N, Jolley D, De Courten M, Shaw J, Zimmet P: High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. Diabetes Care 25:1729-1736, 2002
31. Balducci S, Leonetti F, Di Mario U, Fallucca F: Is a long-term aerobic plus resistance training program feasible for and effective on metabolic profiles in type 2 diabetic patients? Diabetes Care 27:841-842, 2004
32. Bjorgaas M, Vik JT, Saeterhaug A, Langlo L, Sakshaug T, Mohus RM, Grill V: Relationship between pedometer-registered activity, aerobic capacity and self-reported activity and fitness in patients with type 2 diabetes. Diabetes Obes Metab 7:737-744, 2005
33. Loimaala A, Huikuri HV, Koobi T, Rinne M, Nenonen A, Vuori I: Exercise training improves baroreflex sensitivity in type 2 diabetes. Diabetes 52:1837-1842, 2003
34. Maiorana A, O'Driscoll G, Goodman C, Taylor R, Green D: Combined aerobic and resistance exercise improves glycemic control and fitness in type 2 diabetes. Diabetes Res Clin Pract 56:115-123, 2002
35. Tessier D, Menard J, Fulop T, Ardilouze J, Roy M, Dubuc N, Dubois M, Gauthier P: Effects of aerobic physical exercise in the elderly with type 2 diabetes mellitus. Arch Gerontol Geriatr 31:121-132, 2000
36. Dunstan DW, Daly RM, Owen N, Jolley D, Vulikh E, Shaw J, Zimmet P: Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. Diabetes Care 28:3-9, 2005
37. Baum K, Votteler T, Schiab J: Efficiency of vibration exercise for glycemic control in type 2 diabetes patients. Int J Med Sci 4:159-163, 2007
38. van Rooijen AJ, Rheeder P, Eales CJ, Becker PJ: Effect of exercise versus relaxation on haemoglobin A1C in Black females with type 2 diabetes mellitus. Qjm 97:343-351, 2004
39. Kaplan RM, Hartwell SL, Wilson DK, Wallace JP: Effects of diet and exercise interventions on control and quality of life in non-insulin-dependent diabetes mellitus. J Gen Intern Med 2:220-228, 1987
40. Cauza E, Hanusch-Enserer U, Strasser B, Ludvik B, Metz-Schimmerl S, Pacini G, Wagner O, Georg P, Prager R, Kostner K, Dunky A, Haber P: The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. Arch Phys Med Rehabil 86:1527-1533, 2005

41. Vanninen E, Uusitupa M, Siitonen O, Laitinen J, Lansimies E: Habitual physical activity, aerobic capacity and metabolic control in patients with newly-diagnosed type 2 (non-insulin-dependent) diabetes mellitus: effect of 1-year diet and exercise intervention. Diabetologia 35:340-346, 1992
42. Yeater RA, Ullrich IH, Maxwell LP, Goetsch VL: Coronary risk factors in type II diabetes: response to low-intensity aerobic exercise. W V Med J 86:287-290, 1990
43. Bogardus C, Ravussin E, Robbins DC, Wolfe RR, Horton ES, Sims EA: Effects of physical training and diet therapy on carbohydrate metabolism in patients with glucose intolerance and non-insulin-dependent diabetes mellitus. Diabetes 33:311-318, 1984
44. Ligtenberg PC, Hoekstra JB, Bol E, Zonderland ML, Erkelens DW: Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. Clin Sci (Lond) 93:127-135, 1997
45. Thomas D, Elliott E, Naughton G: Exercise for type 2 diabetes mellitus. Cochrane Database Syst Rev 3:CD002968, 2006
46. Snowling NJ, Hopkins WG: Effects of Different Modes of Exercise Training on Glucose Control and Risk Factors for Complications in Type 2 Diabetic Patients: A meta-analysis. Diabetes Care 29:2518-2527, 2006
47. Kelley GA, Kelley KS: Effects of aerobic exercise on lipids and lipoproteins in adults with type 2 diabetes: a meta-analysis of randomized-controlled trials. Public Health 121:643-655, 2007
48. Stratton IM, Cull CA, Adler AI, Matthews DR, Neil HA, Holman RR: Additive effects of glycaemia and blood pressure exposure on risk of complications in type 2 diabetes: a prospective observational study (UKPDS 75). Diabetologia 49:1761-1769, 2006
49. Blair SN, Kohl HW, 3rd, Barlow CE, Paffenbarger RS, Jr., Gibbons LW, Macera CA: Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. Jama 273:1093-1098, 1995
50. Gregg EW, Gerzoff RB, Caspersen CJ, Williamson DF, Narayan KM: Relationship of walking to mortality among US adults with diabetes. Arch Intern Med 163:1440-1447, 2003
51. Whelton SP, Chin A, Xin X, He J: Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 136:493-503, 2002
52. Heritier SR, Gebski VJ, Keech AC: Inclusion of patients in clinical trial analysis: the intention-to-treat principle. Med J Aust 179:438-440, 2003

CHAPTER 3:

Associations between vascular co-morbidities and depression in insulin-naïve diabetes patients. The DIAZOB Primary Care Diabetes study

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ABSTRACT

Objective: the aim of this study was to study the associations between vascular co-morbidity and depression in insulin-naïve patients with type 2 diabetes

Research design and methods: Cross-sectional data from the DIAZOB study were used, involving a primary care sample of 1269 insulin-naïve patients with type 2 diabetes. Demographics, vascular co-morbidities, functional limitations, clinical and lifestyle characteristics, and psychosocial factors were assessed. Depression was assessed with the Edinburgh Depression Scale, a score > 11 was defined as depression. Between-group differences were examined with chi-square statistics and t-tests comparing the groups with and without vascular co-morbidities. Rates and odds ratios of depression were calculated for each vascular co- morbidity, with type 2 diabetes only as the reference group, correcting for age and sex. Finally, sequential multiple regression analyses were performed to test additional, more comprehensive models regarding the risk of depression in diabetes.

Results: Prevalence of depression was 11% in the total sample with no difference between the groups with and without vascular co-morbidities (11.2% versus 10.0%). Except for coronary heart disease and neuropathic foot with coexisting vascular co-morbidities, none of the vascular co-morbidities were significantly associated with depression. The final model predicting depression included having two vascular co-morbidities compared to none, increasing vision problems, difficulties with remembering things, lower social support, having experienced a recent life event, female sex, and smoking.

Conclusions: In the whole sample, rates of depression in those with vascular co-morbidities did not differ from patients with type 2 diabetes only. Vascular co-morbidities were only associated with higher depression scores in case of multiple co-morbidities.

INTRODUCTION

Depression is worldwide one of the leading contributors to the burden of disease, and is an important cause of disability (1). It has been shown that depression is more common in people who have a chronic disease (2). For example, there is mounting evidence that depression is positively associated with type 2 diabetes, the most common type of diabetes. In a recent meta-analysis, Ali et al. (2006) showed that type 2 diabetes significantly increases the prevalence of depression compared to non-diabetic individuals (17.6% vs. 9.8%, OR = 1.3, 95% confidence interval [1.2 – 2.0]) (3). The reasons for this increased prevalence are still not fully understood, but the general notion is that the burden of having diabetes, and particularly having complications of diabetes, plays an important role in the etiology of depression in diabetes. For example, a study in Dutch community dwelling elderly, showed that the prevalence of depression was particularly high in diabetes patients with co-morbid medical disease(s) (20%), compared to patients with type 2 diabetes only (8%) or no chronic disease at all (9%) (4).
De Groot et al. (2001) also showed in their meta-analysis that depression was significantly associated with the presence of several macro- and microvascular diabetes complications (5). Furthermore, there is strong evidence for a relationship between vascular diseases in general and depression, especially in the elderly (6; 7). Additionally, Vileikyte et al. (2005) showed that the severity of diabetic neuropathy was associated with depression, but this relationship was partly mediated by the perceived functional disability when performing daily activities (8). It is important to emphasize that the studies that were included in the meta-analysis of Ali et al. (2006) (3), reported data of relatively small samples of patients with type 2 diabetes. This obviously prevented adequate detection of potential confounding factors in the pooled population.
Little research has been performed in patients with type 2 diabetes in which prevalence of depression is controlled for potential confounders and especially, the co-existence of vascular co- morbidities (4; 9-14). The only large population based primary care sample included in the meta-analysis of Ali et al. (2006) (3) did provide adjusted and unadjusted rates of depression and corrected for cardiovascular disease, but not for other diabetes related complications (15). Additionally, Egede et al. (2005), are probably the only authors who identified the contribution of specific chronic conditions to depression (10). However, their sample did not discriminate between type 1 and type 2 diabetes, and did not examine the contribution of specific co-morbidities to depression. Therefore, the aim of this study was to determine the prevalence of depression in a large, well defined diabetic population of insulin-naïve type 2 diabetes patients, comparing patients with type 2 diabetes only with those with co-existent vascular co-morbidities.

Three research questions were studied:
First, is depression more common in insulin-naïve type 2 diabetes patients with co-existent vascular co-morbidities compared to those who have type 2 diabetes without these co-morbidities?
Second, is the number of vascular co-morbidities associated with higher levels of depression ?
Third, what is the relative contribution of demographic features, clinical and lifestyle factors, and psychosocial factors to depression?

RESEARCH DESIGN AND METHODS

Subjects

Data were collected within a cohort (n = 1770) of patients with type 2 diabetes of a large ongoing diabetes routine care program 'DIAZOB' (Diabetes Care Zuid-Oost Brabant). Subjects living in the Eindhoven region, the Netherlands, were invited by a nurse practitioner trained in diabetes management to join this project during their regular diabetes check-up. The intention is to follow this cohort during their lifetime, and to assess biological, demographic, psychosocial, and lifestyle parameters periodically with a one year time interval. For the purpose of this study, only insulin-naïve patients were included in the analyses, thereby excluding 117 (7%) patients who were using insulin. After exclusion of responders who gave no informed consent (n = 90), and after excluding records due to missing data (n = 294), the study sample included 1269 participants.

Assessments

Demographic variables (age, sex, marital status, educational level), and lifestyle factors (smoking status, and alcohol consumption) were assessed by survey.

Vascular co-morbidities
Vascular co-morbidities, including coronary heart disease (CHD), peripheral arterial disease (PAD), stroke, neuropathic foot, ischemic foot, retinopathy and nephropathy, were assessed during an interview led by the nurse practitioner, who also checked this information in the medical files of the general practitioner.

Functional limitations
Functional limitations were determined using a self-report 5-point Likert scale with a score of 0 indicating 'not at all limited' and a score of 5 indicating 'very much limited' (adapted from the LASA study) (16). The functional limitations that were assessed included: hearing problems, vision problems, miction problems, nocturia, and problems with remembering things.

Other clinical characteristics

HbA_{1c} and body mass index (BMI) values were collected at the Diagnostic Centre Eindhoven, a primary care diagnostic institute which is responsible for the periodic assessment of biological parameters as well as eye and foot examinations in patients with diabetes.

Psychosocial factors

Depression was assessed using the Dutch validated version of the Edinburgh Depression Scale (EDS) (Cronbach's alpha 0.84) (16-19). This is a 10-item self-rating scale in which each item is scored on a four-point Likert scale. Total scores range from 0 to 30 points, with a score of over 11 points indicating the presence of depression. In the present study, cut-off for depression was therefore set at an EDS score of more than 11 points.

Social support was determined by three items adapted from O'Hara et al. (Cronbach's alpha 0.87) (20). Response categories range from 0 to 4 points, with a score of 0 indicating 'no social support at all' and a score of 4 indicating 'extensive social support'. Social support was measured using the sum of the three items.

Furthermore, respondents were asked if they had experienced a stressful life event in the previous 12 months (e.g. loss of a beloved, a divorce, loss of job, serious financial problems or physical/mental abuse).

Statistical analyses

Differences in demographic, clinical and lifestyle characteristics between the group with and without co morbidity were analyzed using chi-square tests (Fisher's exact test when appropriate) for categorical data and student t-tests for continuous data. Logistic regression analyses adjusted for sex and age (ORs with 95% confidence intervals) were performed for each vascular co-morbidity separately with depression as the dependent variable. The group with type 2 diabetes without vascular co morbidities was used as a reference group and was compared with the group with a specific vascular co-morbidity (e.g. stroke) with, and without coexisting vascular diseases. Finally, to assess the relative importance of potential confounders and risk factors of depression, sequential multiple logistic regression analyses (ORs with 95% confidence intervals) were performed in the total group by entering the following sets of independent variables: (1) age, female sex, being single, low education; (2) quantity of vascular co-morbidities; (3) functional limitations; (4) HbA_{1c}, BMI, smoking status, alcohol intake; (5) social support, having experienced a life event recently. Analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 14.

RESULTS

Total sample

The study sample (n=1269) was predominantly Caucasian (97.6%), with an equal sex distribution. The mean age was 66 ± 10 years, and the mean HbA_{1c} level was 6.7%). Prevalence of depression in the total study sample was 11% (males: 6.9%, females: 14.4%, $p < 0.0001$).

Between group differences

The characteristics of the study sample are summarized in Table 1. In total, 562 patients (44%) had type 2 diabetes only, the other 707 (56%) had one or more vascular co-morbidities, of which 431 (61%) had only one vascular disease. The prevalence of macrovascular disease ranged from 6.7 (stroke) to 21.6% (PAD and CHD) of the total sample, whereas microvascular disease was diagnosed in 2.7 % (ischemic foot) to 24.6% (neuropathic foot) of the total sample. As can be seen in Table 1, patients with vascular disease were significantly older, more frequently men, and single and experienced significantly more often functional limitations.

Table 1: Characteristics in subjects without vascular co-morbidity (n = 562) and subjects with vascular co-morbidity (n = 707)

	Type 2 diabetes without vascular co-morbidity	Type 2 diabetes with vascular co-morbidity
	N (%)	N (%)
Demographic features		
Caucasian ethnicity	550 (97.9)	688 (97.3)
Female sex	305 (54.3)	329 (46.5) *
Age (mean, SD)	62.6 (10.1)	68.7 (9.4) **
Low education	343 (61.0)	452 (63.9)
Single status	105 (18.7)	186 (26.3)*
Clinical characteristics		
Diabetes duration (>3 yr)	320 (56.9)	418 (59.1)
Treatment with oral hypoglycemic medication	444 (79.0)	582 (82.3)
HbA_{1c} (mean, SD)	6.6 (0.8)	6.7 (0.8)
Body Mass Index (mean, SD)	29.1 (4.7)	28.8 (4.5)

* *p<0.05*

** *p< 0.0001*

Table 1: continued

	Type 2 diabetes without vascular co-morbidity	Type 2 diabetes with vascular co-morbidity
	N (%)	N (%)
Psychosocial factors		
Depression score EDS (mean, SD)	5.6 (4.7)	5.8 (4.6)
EDS score > 11	56 (10.0)	79 (11.2)
Social support (mean, SD)	7.8 (3.1)	8.1 (2.9) *
Recent life event (previous 12 months)	188 (33.5)	243 (34.4)
Lifestyle factors		
Current smoker	93 (16.5)	97 (13.7)
Alcohol intake (> 14 consumptions/week)	40 (7.1)	54 (7.6)
Functional limitations		
Hearing problems (mean, SD)	0.48 (0.88)	0.76 (1.07) **
Vision problems (mean, SD)	0.72 (0.85)	0.86 (0.93) *
Miction problems (mean, SD)	0.56 (0.91)	0.75 (1.08) *
Nocturia (mean, SD)	0.93 (0.98)	1.17 (1.10) **
Difficulties with remembering things (mean, SD)	0.79 (0.90)	1.01 (1.02) **
Vascular co-morbidities ***		
Macrovascular diseases		457 (36.0)
Peripheral arterial disease	-	274 (21.6)
Coronary disease	-	274 (21.6)
Stroke	-	85 (6.7)
Microvascular diseases		422 (33.3)
Neuropathic foot	-	312 (24.6)
Ischemic foot	-	34 (2.7)
Retinopathy	-	73 (5.8)
Nephropathy	-	482 (3.8)
Number of vascular co-morbidities		
1	-	431 (34.0)
2	-	183 (14.4)
≥ 3	-	93 (7.3)

** p<0.05*

*** p< 0.0001*

**** Vascular co-morbidities: rates are depicted as proportion of total population (n = 1269)*

Prevalence of depression

In a first analysis, the prevalence of depression did not differ significantly between the group of patients without vascular co-morbidities and those with vascular co-morbidities, for the group as a whole (10.0% versus 11.2%, p = 0.49) as well as in men (6.2% versus 7.4%, p = 0.56) and women (13.1 versus 15.5%, p = 0.39) separately. Moreover, more detailed results are shown in Table 2, where the prevalence of depression is shown for each vascular disease. Since 39% of the patients with vascular co-morbidities had multiple vascular co-morbidities, the prevalence of depression is shown for the group with one specific vascular disease only, and the group with this same vascular disease together with one or more coexisting vascular co-morbidities. Except for the group with CHD only (13.3%), and the group with retinopathy only (10.7%), the prevalence of depression tended to be lower in the groups with only one coexisting vascular disease compared to the group having only type 2 diabetes. However, apart from the two above mentioned exceptions, the coexistence of multiple vascular co-morbidities at least doubled the prevalence of depression compared to having only one specific vascular co-morbidity (Table 2).

In Table 2, logistic regression analyses adjusted for sex and age are shown with depression as the dependent variable. For each vascular disease (with and without coexisting vascular diseases) separately, likelihood for depression is compared to having type 2 diabetes without co-morbidities. Vascular co-morbidities that were associated with a substantially higher (i.e. approximately doubled) likelihood of depression were CHD with and without coexisting co-morbidity, and stroke, neuropathic foot, retinopathy and nephropathy in combination with other vascular co-morbidities.

Multiple logistic regression analyses

Finally, the results of sequential multiple logistic regression analyses are shown in Table 3. In the first step, female sex, younger age, and low education were significantly associated with higher levels of depression. In the second step, having two vascular co-morbidities was positively associated with depression, whereas in step three, having vision problems and difficulties with remembering things were associated with higher levels of depression. In the fourth step, none of the added clinical and lifestyle factors appeared to be significantly associated with depression. Ultimately, in the final model (χ^2 9.90, df 8, p = 0.27, Cox & Snell R^2 0.144, Nagelkerke R^2 0.286) depression was significantly predicted by having two vascular co-morbidities (OR = 2.40), increasing vision problems (OR = 1.35) and difficulties with remembering things (OR = 1.69), lower social support (OR = 1.27), having experienced a life event in the previous 12 months year (OR = 2.05), female sex (OR = 3.14), and current smoking (OR = 2.02).

Table 2: Rates and odds for subjects with a specific vascular disease (with and without coexisting vascular diseases) compared to subjects without vascular co-morbidity. Dependent variable: depression (EDS score >11).

			Depression	
	Coexisting vascular diseases	n	Prevalence (%)	Adjusted OR (95% CI) *
Type 2 diabetes only (reference group)	-	562	10.0	1.0
Macrovascular diseases				
Peripheral arterial disease	no	81	6.2	0.61 (0.23 – 1.57)
	yes	193	11.9	1.58 (0.90 – 2.76)
Coronary disease	no	90	13.3	1.72 (0.85 – 3.52)
	yes	184	14.7	**2.03 (1.18 – 3.48)**
Stroke	no	28	7.1	0.87 (0.20 – 3.83)
	yes	57	14.0	2.07 (0.88 – 4.89)
Microvascular diseases				
Neuropathic foot	no	166	9.6	1.22 (0.65 – 2.30)
	yes	146	13.0	**1.87 (1.06 – 3.51)**
Ischemic foot	no	20	5.0	0.70 (0.09 – 5.47)
	yes	14	14.3	1.67 (0.35 – 8.08)
Retinopathy	no	28	10.7	1.02 (0.30 – 3.53)
	yes	45	15.6	2.25 (0.90 – 5.64)
Nephropathy	no	18	5.6	0.58 (0.08 – 4.57)
	yes	30	20.0	2.38 (0.89 – 6.35)

** adjusted for sex and age*

Significant odds ratios are depicted in ***bold***

Table 3: Sequential multiple logistic regression predicting depression by demographic features, vascular co-morbidity, functional limitations, clinical and lifestyle characteristics, and psychosocial factors in insulin-naïve patients with type 2 diabetes (n = 1269)

	Model 1: Demographic features only	Model 2: Number of vascular co-morbidities controlled for demographics	Model 3: Associations with demographics, vascular co-morbidities, and functional limitations	Model 4: Associations with demographics, vascular co-morbidities functional limitations, clinical and lifestyle characteristics	Model 5: Final model, plus social support and experience of a recent life event
I Demographic features					
Age	**0.98 (0.96 – 0.99)**	**0.97 (0.95 – 0.99)**	**0.96 (0.94 – 0.98)**	**0.96 (0.93 – 0.98)**	0.96 (0.95 – 1.00)
Female sex	**2.34 (1.49 – 3.66)**	**2.54 (1.61 – 4.02)**	**2.57 (1.59 – 4.17)**	**2.65 (1.61 – 4.37)**	**3.14 (1.85 – 5.34)**
Being single	1.39 (0.86 - 2.24)	1.34 (0.82 – 2.17)	1.34 (0.80 – 2.25)	1.34 (0.79 – 2.26)	1.28 (0.74 – 2.21)
Low education	**1.64 (1.01 – 2.66)**	**1.64 (1.01 – 2.67)**	1.34 (0.80 – 2.24)	1.30 (0.77 – 2.19)	1.10 (0.64 – 1.88)
II Vascular co-morbidities					
0		1.00	1.00	1.00	1.00
1		0.94 (0.56 – 1.56)	0.80 (0.47 – 1.38)	0.79 (0.46 – 1.37)	0.92 (0.52 – 1.62)
2		2.15 (1.20 – 3.86)	1.93 (1.04 – 3.59)	2.00 (1.07 – 3.74)	2.40 (1.25 – 4.62)
≥ 3		1.81 (0.80 – 4.10)	1.48 (0.62 – 3.53)	1.56 (0.65 – 3.75)	1.75 (0.70 – 4.36)

Table 3: continued

III Functional limitations					
Hearing problems			0.93 (0.74 – 1.18)	0.94 (0.74 – 1.19)	0.93 (0.73 – 1.18)
Vision problems			**1.36 (1.07 – 1.73)**	**1.36 (1.07 – 1.74)**	**1.35 (1.05 – 1.74)**
Miction problems			1.11 (0.88 – 1.40)	1.11 (0.88 – 1.41)	1.13 (0.88 – 1.45)
Nocturia			1.03 (0.82 – 1.31)	1.05 (0.83 – 1.33)	1.01 (0.79 – 1.29)
Difficulties with remembering things			**1.74 (1.40– 2. 15)**	**1.70 (1.36 – 2.12)**	**1.69 (1.35 – 2.13)**
IV Clinical and lifestyle factors					
Treatment with oral hypoglycemic medication				1.02 (0.57 – 1.84)	0.87 (0.47 – 1.61)
Higher HbA_{1c}				0.93 (0.69 – 1.26)	0.91 (0.66 – 1.26)
Higher BMI				0.96 (0.92 – 1.01)	0.97 (0.93 – 1.02)
Current smoker				1.59 (0.92 – 2.75)	**2.02 (1.14 – 3.58)**
Alcohol intake > 14 consumptions / week				0.61 (0.22 – 1.66)	0.73 (0.26 – 2.06)
V Psychosocial factors					
Lower social support					**1.27 (1.17 – 1.37)**
Recent life event					**2.05 (1.28 – 3.27)**
Goodness of fit (χ2 (df), P-value)	3.45 (8), p = 0.90	4.34 (8), p = 0.83	10.29 (8), p = 0.25	11.86 (8), p = 0.16	9.90 (8), p = 0.27

*ORs and 95% CIs depicted in **bold** are significant*

DISCUSSION

In the present study, the prevalence of depression in insulin-naïve type 2 diabetes patients was 11%, which was lower than the prevalence (17%) reported in the meta-analysis of Ali et al. (2006) and the rates reported in two previous studies in Dutch type 2 diabetes patients (3, 4, 14). It was even comparable to the prevalence of depression in non-diabetic individuals and type 2 diabetes patients without co-morbidities (3; 4). Furthermore, results of our study show that the prevalence of depression was not increased in the whole group of type 2 diabetes patients with co-morbidities (even when stratified for sex).

Further more detailed analyses, though, demonstrated that the presence of multiple vascular co-morbidities approximately doubled the likelihood of depression. In line with findings of previous research (4; 10; 12; 21), the number of vascular co-morbidities was related to higher levels of depression. For example, Rubin et al. (1997) found that in patients with three or more vascular co-morbidities, the risk of developing depression was increased (21). However, in the study of Katon et al. (2004), in which also patients with type 1 diabetes were included, the number of diabetes co-morbidities was associated with major depression in men only, and with minor depression in older patients only (12) .

We believe that there are several possible explanations for our finding that depression was more common in patients with multiple co-morbidities. First, the burden of having several chronic diseases might have contributed to feelings of depression. Secondly, there may also be biological mechanisms that are associated with cardiovascular disease that can also contribute to depression. For example: an increasing number of studies suggest that inflammatory responses have an important role in the pathophysiology of type 2 diabetes, cardiovascular disease and depression. An ongoing cytokine-induced acute phase response appears to be closely involved in the pathogenesis of type 2 diabetes and associated complications (22). Considerable evidence has accumulated over the past decade that the atherosclerotic process is regulated by inflammatory mechanisms. Cardiovascular disease is increasingly being viewed as a chronic inflammatory response to injuries of the vascular endothelium (23). In the field of psychiatry, depressed patients have been found to have higher levels of cytokines, acute phase proteins, chemokines and cellular adhesion molecules. In addition, an association between immune activation and depression is supported by studies describing a very high incidence of depressive symptoms (50%) in patients undergoing immunostimulatory therapies such as interferon alpha for hepatitis C or IL-6 and IL-2 for cancer (24).

It should be noticed that the current primary care sample consisted of insulin-naïve patients with a relatively "uncomplicated" diabetes. As could be expected, the proportion of patients with vascular co-morbidities was still relatively low (56%). In other studies percentages of patients with co-morbid disease typically ranged from 69-75% (4; 10-12). Furthermore, the current study confirmed previous findings that functional limitations, which often come along with old age and chronic diseases such as cardiovascular disease, increase the likelihood of depression (4; 11). Except for the number of vascular co-morbidities, no other diabetes-specific factors were associated with depression. This is in contrast for example with conclusions of a meta-analysis showing that elevated HbA_{1c} levels were associated with higher levels of depression (25). We believe this may be due to the relatively good glycemic control in our sample. Similarly, BMI was not associated with depression, which is also in contrast with previous studies (12; 15). Finally, in the current study the low levels of social support and the occurrence of major life events were also strongly associated with depression, which has also been reported in the literature of depression in general.

A major strength of our study is the detailed documentation of the presence of vascular co-morbidities. Other strengths are the relatively large sample size and the homogeneous character of the sample of insulin-naïve patients with type 2 diabetes. However, some limitations need to be mentioned. First, the cross-sectional design does not allow for making causal inferences, such as statements on whether co-morbidities and functional limitations preceded depression or vice versa. Second, although the total sample was relatively large, it was difficult to identify the contribution to depression of the individual vascular co- morbidities, since they are often accompanied with other vascular co-morbidities. Thirdly, the burden of having vascular co-morbidities may not fully be evaluated by our measure of functional limitations. Future studies should also include limitations such as decreased mobility and disability when performing daily and/or social activities, and/or diabetes symptoms which may be assessed by the Diabetes Symptom Checklist (26). Finally, depressive symptoms rather than syndromal depression were assessed. For obvious reasons, in large samples, self-rating scales are preferentially used.

In conclusion, in the current, relatively healthy, primary care sample, rates of depression in patients with vascular co-morbidities were not higher than in patients with type 2 diabetes without vascular co-morbidities. However, more detailed analyses showed that having two or more vascular co-morbidities, and in particular coronary heart disease or neuropathic foot combined with other vascular diseases, increased the risk of depression compared to having type 2 diabetes without vascular co-morbidities.

REFERENCES

1. Michaud CM, Murray CJ, Bloom BR: Burden of disease--implications for future research. Jama 285:535-539, 2001
2. Bisschop MI, Kriegsman DM, Deeg DJ, Beekman AT, van Tilburg W: The longitudinal relation between chronic diseases and depression in older persons in the community: the Longitudinal Aging Study Amsterdam. J Clin Epidemiol 57:187-194, 2004
3. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K: The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med 23:1165-1173, 2006
4. Pouwer F, Beekman AT, Nijpels G, Dekker JM, Snoek FJ, Kostense PJ, Heine RJ, Deeg DJ: Rates and risks for co-morbid depression in patients with Type 2 diabetes mellitus: results from a community-based study. Diabetologia 46:892-898, 2003
5. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ: Association of depression and diabetes complications: a meta-analysis. Psychosom Med 63:619-630, 2001
6. Camus V, Kraehenbuhl H, Preisig M, Bula CJ, Waeber G: Geriatric depression and vascular diseases: what are the links? J Affect Disord 81:1-16, 2004
7. Thomas AJ, Kalaria RN, O'Brien JT: Depression and vascular disease: what is the relationship? J Affect Disord 79:81-95, 2004
8. Vileikyte L, Leventhal H, Gonzalez JS, Peyrot M, Rubin RR, Ulbrecht JS, Garrow A, Waterman C, Cavanagh PR, Boulton AJ: Diabetic peripheral neuropathy and depressive symptoms: the association revisited. Diabetes Care 28:2378-2383, 2005
9. de Jonge P, Roy JF, Saz P, Marcos G, Lobo A: Prevalent and incident depression in community-dwelling elderly persons with diabetes mellitus: results from the ZARADEMP project. Diabetologia 49:2627-2633, 2006
10. Egede LE: Effect of comorbid chronic diseases on prevalence and odds of depression in adults with diabetes. Psychosom Med 67:46-51, 2005
11. Engum A, Mykletun A, Midthjell K, Holen A, Dahl AA: Depression and diabetes: a large population-based study of sociodemographic, lifestyle, and clinical factors associated with depression in type 1 and type 2 diabetes. Diabetes Care 28:1904-1909, 2005
12. Katon W, von Korff M, Ciechanowski P, Russo J, Lin E, Simon G, Ludman E, Walker E, Bush T, Young B: Behavioral and clinical factors associated with depression among individuals with diabetes. Diabetes Care 27:914-920, 2004
13. Knol MJ, Heerdink ER, Egberts AC, Geerlings MI, Gorter KJ, Numans ME, Grobbee DE, Klungel OH, Burger H: Depressive symptoms in

subjects with diagnosed and undiagnosed type 2 diabetes. Psychosom Med 69:300-305, 2007
14. Pawaskar MD, Anderson RT, Balkrishnan R: Self-reported predictors of depressive symptomatology in an elderly population with type 2 diabetes mellitus: a prospective cohort study. Health Qual Life Outcomes 5:50, 2007
15. Nichols GA, Brown JB: Unadjusted and adjusted prevalence of diagnosed depression in type 2 diabetes. Diabetes Care 26:744-749, 2003
16. Beekman AT, Deeg DJ, van Tilburg T, Smit JH, Hooijer C, van Tilburg W: Major and minor depression in later life: a study of prevalence and risk factors. J Affect Disord 36:65-75, 1995
17. Cox JL, Chapman G, Murray D, Jones P: Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. J Affect Disord 39:185-189, 1996
18. Cox JL, Holden JM, Sagovsky R: Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 150:782-786, 1987
19. Pop VJ, Komproe IH, van Son MJ: Characteristics of the Edinburgh Post Natal Depression Scale in The Netherlands. J Affect Disord 26:105-110, 1992
20. O'Hara MW: Social support, life events, and depression during pregnancy and the puerperium. Arch Gen Psychiatry 43:569-573, 1986
21. Rubin RR: Psychotherapy in Diabetes Mellitus. Semin Clin Neuropsychiatry 2:72-81, 1997
22. Pickup JC: Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes Care 27:813-823, 2004
23. Ross R: Atherosclerosis--an inflammatory disease. N Engl J Med 340:115-126, 1999
24. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW: From inflammation to sickness and depression: when the immune system subjugates the brain. Nat Rev Neurosci 9:46-56, 2008
25. Lustman PJ, Clouse RE: Depression in diabetic patients: the relationship between mood and glycemic control. J Diabetes Complications 19:113-122, 2005
26. Grootenhuis PA, Snoek FJ, Heine RJ, Bouter LM: Development of a type 2 diabetes symptom checklist: a measure of symptom severity. Diabet Med 11:253-261, 1994

CHAPTER 4:

Depression is associated with physical inactivity in patients with type 2 diabetes

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ABSTRACT

Background: Prevalence of physical inactivity in individuals with type 2 diabetes is high. Little information is known about the factors associated with physical inactivity.

Objective: To examine possible factors related to physical inactivity in individuals with type 2 diabetes, taking into account a set of psychosocial factors.

Methods: Individuals with type 2 diabetes from 100 general practitioners in the Eindhoven region, the Netherlands, were invited to join this study by a nurse practitioner during regular diabetes check up. In 2646 primary care type 2 diabetes patients who responded, demographic variables, physical inactivity, health related factors, lifestyle factors and psychosocial factors were analyzed. Single and multiple logistic regression analyses (OR, 95% CI) were performed with physical inactivity as the dependent variable.

Results: About 48% of the respondents were physically inactive. Signs of depression were found in 14% of the respondents. Multiple logistic regression analyses showed that physical inactivity was significantly associated with depression (OR = 1.67, 95% CI 1.24 – 2.24), being single (OR = 1.27, 95% CI 1.01 – 1.59), female sex (OR = 1.24, 95% CI 1.02 – 1.52), higher body mass index (OR = 1.04, 95% CI 1.02 – 1.06), and older age (OR = 1.02, 95% CI 1.01 – 1.03).

Conclusions: Depression is an important factor related to physical inactivity in individuals with type 2 diabetes.

INTRODUCTION

Increased wealth in Western countries is reflected in a longer lifetime, a high prevalence of overweight and physical inactivity. One of the most important consequences of these developments is a strong rise in the prevalence of type 2 diabetes. In the Netherlands, the annual prevalence of type 2 diabetes was estimated in 2003 to be 34.6 per 1000 (n = 287,200) for men and 36.3 per 1000 (n = 297,700) for women (1). Solely based on demographic data, the prevalence of diabetes is expected to increase by 32.5% between 2005 and 2025. However, this increase may be even greater since the prevalence of overweight is rising (2). Type 2 diabetes is a complex chronic disease with high co-morbidity. Diabetes management aims at achieving and maintaining glycemic control and reducing cardiovascular risk factors in order to prevent or delay vascular and neural complications. Disease control is largely influenced by lifestyle habits and self-care, which places great demands on the patient's self-management capabilities (3).

Physical activity is an important aspect of diabetes management since it has a positive effect on glycemic control as well as on cardiovascular risk (4). However, inactivity is high in type 2 diabetes patients (4; 5). Physical activity behavior is very complex and depends on several factors. The strongest and most consistent associations are found between physical activity and demographic features. Physically active people are more likely to be male, younger, and higher educated (6). Furthermore, physical activity depends on several physical (e.g. prevalence of overweight/obesity and co-morbidities), psychosocial (e.g. mood, social support, self-efficacy), and environmental factors (e.g. time and access to exercise facilities) (6; 7).

Research concerning the factors related to physical activity in type 2 diabetes patients is scarce (8-15). Possible related factors assessed have predominantly included demographic factors (age, sex, ethnicity, marital status, education level, income), body mass index, and prevalence of physical limitations. The results of these studies are inconsistent due to a variety of sample characteristics and methodological considerations (14), and are difficult to compare because different measures of physical activity and different independent variables were used. Furthermore, little is known about the causality of the reported associations, since only two studies applied a longitudinal design (12; 13).

Diabetes is often accompanied by psychosocial problems, such as depression and anxiety (16; 17). Coping with diabetes is psychologically and behaviorally challenging, and psychosocial factors may therefore influence almost all aspects of disease management (16). There was hardly any assessment of psychosocial factors in the existing studies, however. Only Lin et al. (9) and Morrato et al. (10) included depression as a possible factor related to physical activity. Both studies found depression to be a strong correlate of physical activity in individuals with type 2 diabetes.

However, the effect of other psychosocial factors such as social support and loneliness has not yet been studied in type 2 diabetes populations. Therefore, the aim of this study was to examine factors related to physical inactivity in individuals with type 2 diabetes, taking into account a set of psychosocial factors.

METHODS

Subjects

Between January and April 2006, a number of 3300 individuals with type 2 diabetes from 100 general practitioners in the Eindhoven region, the Netherlands, were asked to join this study by a nurse practitioner during their regular diabetes check-up. The current study is the first of an ongoing diabetes management project called 'DIAZOB'. In this project, the cohort will be followed during their lifetime and will be periodically assessed for biological parameters and demographic, psychosocial, and lifestyle parameters. After exclusion of responders who gave no informed consent, and after excluding records due to missing data, 2646 participants were included in the final analysis (response rate after exclusion: 80%).

Assessments

Besides physical inactivity, several factors related to physical activity, as described in the literature (6; 7), were assessed by survey at baseline. Those factors included demographics (ethnicity, age, sex, level of education, and marital status), clinical characteristics (duration of diabetes, diabetes treatment, HbA_{1c} level, and body mass index), and lifestyle factors (smoking status and alcohol intake). Furthermore, three psychosocial factors were included, namely depression, loneliness, and social support.

Physical inactivity

Physical activity was assessed during a nurse-led interview. The nurse practitioner asked the patient how many hours per week s/he spends on 'active' physical activity (like walking, cycling, stair climbing, gardening, etcetera., other than sports). Answer categories were: 'never', '1-2 hours', '>2-4 hours', '>4-6 hours', and 'over 6 hours' per week. Respondents who said they were physically active for 4 or less hours per week were labeled 'inactive', the others as 'active'.

Psychosocial factors

Depression was assessed using a validated Dutch version of the Edinburgh Depression Scale (EDS) (18-20). This is a 10-item self-rating scale in which each item is scored on a four-point Likert scale. Total scores range from 0 to 30 points, with a score of over 11 points indicating the presence of depression. In the present study, cut-off for depression was therefore set at an EDS score of more than 11 points.

Social support was determined by three items adapted from O'Hara et al. (21). Answer categories ranged from 0 to 4 points, with 0 indicating 'no social support at all' and 4 indicating 'extensive social support'. Social support was scored by the sum of the three items. Low levels of social support were defined by the mean score minus one standard deviation.
Feelings of loneliness during the last 12 months were scored on a scale from 1 to 10 points, with a score of 1 meaning 'never feel lonely' and a score of 10, 'always feel lonely'. High levels of loneliness were defined by the mean score plus one standard deviation.
All data were patient reported by means of a survey, except for HbA_{1c} and body mass index values which were collected at the Diagnostic Centre Eindhoven, a primary care diagnostic institute. The biological factors were assessed at the same time as the survey.

Statistical analyses

Analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 14. After checking for normality, and colinearity, single and multiple logistic regression analyses (OR, 95% CI) were performed with physical activity as the dependent variable. All variables were simultaneously entered in the multiple analysis. No comparisons were made between responders and non-responders.

RESULTS

The characteristics of the study sample are summarized in table 1. The sample was predominantly Caucasian (98%), with a roughly equal sex distribution. The average age was 68 years, and the average HbA_{1c} level was 6.7%). Some 48% of the respondents was classified as physically inactive. Signs of depression were found in 14% of all respondents.

Table 1: Characteristics of respondents (n = 2646)

	N (%)
Demographic features	
Caucasian ethnicity	2434 (97.5)
Female sex	1345 (50.8)
Age (mean, SD)	67.7 (10.5)
Educational level	
Low	1641 (62.0)
Middle	643 (24.3)
High	270 (10.2)
Academic	92 (3.5)
Single status	713 (26.9)
Clinical characteristics	
Diabetes duration (mean, SD)	6.3 (6.2)
Treatment	
Diet	478 (18.1)
Oral therapy	1924 (72.7)
Oral therapy and insulin	189 (7.1)
Insulin	55 (2.1)
HbA_{1c} (mean, SD)	6.7 (0.7)
Body Mass Index (mean, SD)	29.6 (4.8)
Psychosocial factors	
Depression score EDS (mean, SD)	5.9 (4.9)
EDS score > 11	360 (13.6)
Low levels of social support	451 (17.0)
Increased levels of loneliness	482 (18.2)
Lifestyle factors	
Physically inactive (≤ 4 hours / week)	1284 (48.5)
Alcohol intake (> 14 consumptions / week)	139 (5.3)
Smoking	393 (14.9)

In table 2, single logistic regression analyses show that depression (OR = 1.93, 95% CI 1.54 – 2.43), high levels of loneliness (OR = 1.55, 95% CI 1.27 – 1.90), being single (OR = 1.56, 95% CI 1.32 – 1.86), low levels of social support (OR = 0.80, 95% CI 0.65 – 0.98), female sex (OR = 1.54, 95% CI 1.32 – 1.80), higher body mass index (OR = 1.03, 95% CI 1.02 – 1.05), and older age (OR = 1.01, 95% CI 1.01 – 1.02) were significantly associated with physical inactivity.

Table 2: Single logistic regression analysis (n = 2646). Dependent variable: physical inactivity (OR, 95% CI)

	OR (95% CI)
Demographic features	
Female sex	**1.54 (1.32 – 1.80)**
Older age	**1.01 (1.01 – 1.02)**
Low educational level	0.91 (0.77 – 1.07)
Single status	**1.56 (1.32 – 1.86)**
Health status	
Higher body mass index	**1.03 (1.02 – 1.05)**
Psychosocial features	
Depression (EDS score > 11)	**1.93 (1.54 – 2.43)**
Low levels of social support	**0.80 (0.65 – 0.98)**
Increased levels of loneliness	**1.55 (1.27 – 1.90)**
Lifestyle habits	
Smoking	0.99 (0.80 – 1.23)
Alcohol intake	0.85 (0.60 – 1.19)

*ORs and 95% CIs depicted in **bold** are significant*

The results of the multiple logistic regression are shown in table 3. Significant associations of physical inactivity were depression (OR = 1.67, 95% CI 1.24 – 2.24), being single (OR = 1.27, 95% CI 1.01 – 1.59), female sex (OR = 1.24, 95% CI 1.02 – 1.52), higher body mass index (OR = 1.04, 95% CI 1.02 – 1.06), and older age (OR = 1.02, 95% CI 1.01 – 1.03).

Table 3: Multiple logistic regression analysis (n = 2646).
Dependent variable: physical inactivity (OR, 95% CI).
All single variables are entered in multiple analysis

	OR (95% CI)
Demographic features	
Female sex	**1.24 (1.02 – 1.52)**
Older age	**1.02 (1.01 – 1.03)**
Low educational level	1.12 (0.91 – 1.38)
Single status	**1.27 (1.01 – 1.59)**
Health status	
Higher body mass index	**1.04 (1.02 – 1.06)**
Psychosocial features	
Depression (EDS score > 11)	**1.67 (1.24 – 2.24)**
Low levels of social support	0.84 (0.66 – 1.08)
Increased levels of loneliness	1.18 (0.91 – 1.54)
Lifestyle habits	
Smoking	1.09 (0.83 – 1.43)
Alcohol intake	0.93 (0.61 – 1.41)

*ORs and 95% CIs depicted in **bold** are significant*
Method: Enter

DISCUSSION

This study examined the association between physical inactivity and psychosocial factors in a cohort of adults with type 2 diabetes in primary care. Diabetes is often accompanied by psychosocial problems such as depression (16; 17), and these factors in turn may negatively affect health behaviors (22). Some 41% of the respondents was physically inactive. The prevalence of depression in the entire sample was 12.1%. This is somewhat lower than that reported in the meta-analysis of Ali et al. (18), who found a prevalence of 17.6% in people with type 2 diabetes (n = 18,455). In line with the previous work of Lin et al. (9) and Morrato et al. (10) in adults with type 2 diabetes, depression was an important factor related to physical inactivity in this study. Although there is significant evidence for the negative association of loneliness and several adverse health outcomes (23), the current study supports the findings of previous research addressing to loneliness and physical activity, in which no association was found between both variables

(23) (24). Furthermore, in line with studies in older adults (25-28) but in contrast to Plotnikoff et al. (14), participants without a partner were more likely to report lower physical activity than those with a partner. The outcomes of the current study support the findings of previous studies in patients with type 2 diabetes, which showed that women (11; 12; 14) and elderly people (8; 10-12; 14) were less likely to be physically active, associations that have been consistently demonstrated in the general population (6; 7). However, other studies in adults with type 2 diabetes did not find differences between sexes (8; 10; 11; 13; 15) or across age groups (13; 15).

Furthermore, higher BMI was associated with physical inactivity. Overweight is common in type 2 diabetes and an important barrier to physical activity (6; 7). Two out of the five other studies that examined the association of BMI and physical activity in patients with type 2 diabetes also found a positive relationship. Two studies did not find an association due to methodological restrictions (8; 11). Nor did Plotnikoff et al. detect an association between BMI and physical activity in their static model (13). However, in the longitudinal model covering a period of six months, persons with a high BMI were more likely to become physically active, which may be a temporary effect of the first assessment which increased their motivation to change their behavior, especially in newly diagnosed patients.

The strengths of this study are the large number of diabetes patients included and, the study of psychological variables in the real world setting of diabetes care. However, this study also has some limitations. Due to its cross-sectional design, no causal relationships could be determined between physical inactivity and the hypothesized determinants. Longitudinal data are needed to test the causality of the associations found in the multiple regression model. Another limitation involved the self-reporting of physical activity. The single item by which physical activity was assessed was phrased in general terms and did not include information about intensity, which probably encouraged overestimation. Furthermore, the current study did not account for physical limitations, which are often present in type 2 diabetes patients and may impose physical inactivity (10; 13).

Understanding the role of physical, psychosocial, and environmental factors related to physical activity is important to obtain profiles of people who may be at risk of physical inactivity, or more likely to give up physical activity. These groups of people may require specific attention and tailored interventions.

Psychosocial problems may negatively influence physical activity levels, while on the other hand, high levels of physical activity may positively influence psychosocial problems as well, and may have a positive effect on well-being. For example, a randomized, controlled trial in older adults participating in a 6-month exercise program noted a decrease in symptoms of depression, and this reduction was sustained after 12 months and even 60 months from baseline. Participation in the exercise program buffered feelings of loneliness by providing social resources, but this effect was not sustained in the six months after the end of the program (29, 30).

The findings of the current study provide only a preliminary contribution towards understanding the association of depression and physical activity in individuals with type 2 diabetes. Longitudinal studies and randomized controlled trials are needed to identify the nature and magnitude of this association.

REFERENCES

1. Lisdonk EHvd, Bosch WJHM vd, Huygen FJA: Ziekten in de huisartsenpraktijk. Utrecht, Bunge, 2003
2. Baan CA, Rijken PM: Volksgezondheid Toekomstverkenning, Nationaal Kompas Volksgezondheid. Bilthoven, RIVM, 2005
3. Snoek FJ: Breaking the barriers to optimal glycaemic control--what physicians need to know from patients' perspectives. Int J Clin Pract Suppl:80-84, 2002
4. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C: Physical activity/exercise and type 2 diabetes. Diabetes Care 27:2518-2539, 2004
5. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
6. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W: Correlates of adults' participation in physical activity: review and update. Med Sci Sports Exerc 34:1996-2001, 2002
7. Sherwood NE, Jeffery RW: The behavioral determinants of exercise: implications for physical activity interventions. Annu Rev Nutr 20:21-44, 2000
8. Hays LM, Clark DO: Correlates of physical activity in a sample of older adults with type 2 diabetes. Diabetes Care 22:706-712, 1999
9. Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B: Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care 27:2154-2160, 2004
10. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW: Physical activity in U.S. adults with diabetes and at risk for developing diabetes, 2003. Diabetes Care 30:203-209, 2007
11. Nelson KM, Reiber G, Boyko EJ: Diet and exercise among adults with type 2 diabetes: findings from the third national health and nutrition examination survey (NHANES III). Diabetes Care 25:1722-1728, 2002
12. Nothwehr F, Stump T: Health-promoting behaviors among adults with type 2 diabetes: findings from the Health and Retirement Study. Prev Med 30:407-414, 2000
13. Plotnikoff RC, Lippke S, Karunamuni N, Eves N, Courneya KS, Sigal R, Birkett NJ: Co-morbidity, functionality and time since diagnosis as predictors of physical activity in individuals with type 1 or type 2 diabetes. Diabetes Res Clin Pract 78:115-122, 2007
14. Plotnikoff RC, Taylor LM, Wilson PM, Courneya KS, Sigal RJ, Birkett N, Raine K, Svenson LW: Factors associated with physical activity in Canadian adults with diabetes. Med Sci Sports Exerc 38:1526-1534, 2006

15. Spangler JG, Konen JC: Predicting exercise and smoking behaviors in diabetic and hypertensive patients. Age, race, sex, and psychological factors. Arch Fam Med 2:149-155, 1993
16. Delamater AM, Jacobson AM, Anderson B, Cox D, Fisher L, Lustman P, Rubin R, Wysocki T: Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. Diabetes Care 24:1286-1292, 2001
17. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE: Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. Diabet Med 22:1379-1385, 2005
18. Cox JL, Holden JM, Sagovsky R: Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 150:782-786, 1987
19. Cox JL, Chapman G, Murray D, Jones P: Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. J Affect Disord 39:185-189, 1996
20. Pop VJ, Komproe IH, van Son MJ: Characteristics of the Edinburgh Post Natal Depression Scale in The Netherlands. J Affect Disord 26:105-110, 1992
21. O'Hara MW: Social support, life events, and depression during pregnancy and the puerperium. Arch Gen Psychiatry 43:569-573, 1986
22. Piette JD, Richardson C, Valenstein M: Addressing the needs of patients with multiple chronic illnesses: the case of diabetes and depression. Am J Manag Care 10:152-162, 2004
23. Lauder W, Mummery K, Jones M, Caperchione C: A comparison of health behaviours in lonely and non-lonely populations. Psychol Health Med 11:233-245, 2006
24. Lampinen P, Heikkinen RL, Kauppinen M, Heikkinen E: Activity as a predictor of mental well-being among older adults. Aging Ment Health 10:454-466, 2006
25. Pettee KK, Brach JS, Kriska AM, Boudreau R, Richardson CR, Colbert LH, Satterfield S, Visser M, Harris TB, Ayonayon HN, Newman AB: Influence of marital status on physical activity levels among older adults. Med Sci Sports Exerc 38:541-546, 2006
26. Satariano WA, Haight TJ, Tager IB: Living arrangements and participation in leisure-time physical activities in an older population. J Aging Health 14:427-451, 2002
27. Schone BS, Weinick RM: Health-related behaviors and the benefits of marriage for elderly persons. Gerontologist 38:618-627, 1998
28. Kharicha K, Iliffe S, Harari D, Swift C, Gillmann G, Stuck AE: Health risk appraisal in older people 1: are older people living alone an "at-risk" group? Br J Gen Pract 57:271-276, 2007

29. McAuley E, Blissmer B, Marquez DX, Jerome GJ, Kramer AF, Katula J: Social relations, physical activity, and well-being in older adults. Prev Med 31:608-617, 2000
30. Motl RW, Konopack JF, McAuley E, Elavsky S, Jerome GJ, Marquez DX: Depressive symptoms among older adults: long-term reduction after a physical activity intervention. J Behav Med 28:385-394, 2005

CHAPTER 5:

Type D personality is related to physical inactivity and depression in adults with type 2 diabetes

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ABSTRACT

Aims/hypothesis: The aim of this study was to examine (a) the prevalence of the distressed or Type D personality (high negative affectivity and social inhibition) in a type 2 diabetes population, and (b) the effect of the Type D personality on both physical inactivity and depression as diabetic risk factors.

Methods: 2556 primary care type 2 diabetes patients were assessed on Type D personality, physical inactivity, presence of depression, demographics, smoking status, and alcohol intake. A validation study was performed to examine the internal validity and consistency of the Type D assessment (DS14 questionnaire) in the diabetes population. Single and multiple regression analyses (OR, 95% CI) were performed, with physical inactivity as well as depression as the dependent variable.

Results: In all, 21% of the individuals with type 2 diabetes had a Type D personality. After adjustment for sex, age, and lifestyle factors, Type D individuals had increased likelihoods for physical inactivity (56%) compared with non-Type D individuals (47%); OR = 1.40, 95% CI 1.15 – 1.70, $p<0.0001$. Type D individuals had a seven-fold increased likelihood of experiencing symptoms of depression (37% of cases) compared with non-Type D individuals (7%) when corrected for demographic and lifestyle factors; OR = 7.41, 95% CI 5.79 – 9.49, $p<0.0001$.

Conclusions/interpretation: It may be useful to identify Type D individuals in diabetes practice, since Type D personality is associated with both depression and physical inactivity. These individuals may be followed intensively to monitor lifestyle and self-management.

INTRODUCTION

Physical activity has proven to be effective in the prevention and disease management of type 2 diabetes (1; 2). However, prevalence of physical inactivity is high amongst individuals with type 2 diabetes, and long-time adherence to physical activity programs is low (1; 3). Therefore, it is important to know the determinants of physical inactivity, in order to identify individuals at risk. This knowledge can be used to indicate targets for physical activity promotion in diabetes care practice and hence to increase the effectiveness of physical activity interventions.

A large body of research is available concerning factors determining physical activity, including demographic, environmental, lifestyle, and psychosocial factors (4; 5). One of the psychosocial factors shown to be related to physical inactivity in the general population (6; 7), as well as in adults with type 2 diabetes, is the presence of depression (8). Another psychosocial factor that has been studied in this light is personality. In their meta-analysis on personality determinants of physical activity, Rhodes and Smith identified extraversion and conscientiousness as positive correlates, while neuroticism was shown to be a negative correlate (9).

A personality trait that has been the focus of increasing attention in the context of cardiovascular disease is the Type D personality. This is a distressed personality and is defined as the tendency to experience increased negative emotions (negative affectivity) paired with a lack of expression of these emotions in social interactions (social inhibition) (10). Previous studies on this concept concerned several cardiovascular conditions, since psychologic stress has been shown to be a risk factor for these diseases (11; 12). The prevalence of Type D personality ranged between 24% and 34% (coronary artery disease), and 33 – 53% (hypertension, peripheral arterial disease, and chronic heart failure) (13). Type D individuals showed an inadequate response to cardiac treatment and had an increased risk of morbidity and mortality (12).

However, no studies to date have examined the Type D personality construct in the context of diabetes. This is an important issue since type 2 diabetes patients have an increased risk of cardiovascular disease (14; 15). In clinical practice, a Type D personality may manifest in poor consultation behavior, and hence poor self-management, due to the tendency of Type D individuals to inhibit self-expression in social interactions (16). Self-management is an essential element in the management of type 2 diabetes and concerns the use of medication as well as lifestyle interventions, such as diet and physical activity (8). Furthermore, the Type D personality has been shown to be related to depression (10; 17), which is significantly more prevalent in persons with type 2 diabetes than in the general population (18; 19), and is also related to poor self-management (20-22).

Since this is the first study to examine Type D personality in persons with type 2 diabetes, the aim of the present study was twofold. First, to examine the validity and prevalence of Type D personality in persons with type 2 diabetes. Second, to examine the effect of Type D personality on physical inactivity and depression as major diabetic risk factors.

METHODS

Subjects

Between January and April 2006, a population of 3300 individuals with type 2 diabetes in the Eindhoven region, the Netherlands, was invited during regular diabetes check-ups by their nurse practitioner to join an ongoing diabetes management project called 'DIAZOB'. The for this purpose assembled cohort will be followed during their lifetime and will be periodically assessed for biological parameters and demographic, psychosocial, and lifestyle parameters in a patient survey. All participants gave written informed consent. After exclusion of records due to missing data, 2556 participants were included in the final analysis (response rate after exclusion: 77%).

Clinical characteristics

Assessed demographic variables included sex, age, marital status, and education level. The clinical characteristics included HbA_{1c} level (%), and the lifestyle factors included smoking status and alcohol intake. All variables were patient-reported, except for HbA_{1c} values, which were measured at the Diagnostic Centre Eindhoven, the Netherlands, a primary care diagnostic institute.

Type D personality

Type D personality was assessed using the Type D Scale-14 (DS14) (12). This questionnaire consists of 14 items which are scored on a five-point Likert-scale ranging from 0 = 'false' to 4 = 'true'. The DS14 comprises two scales, one measuring levels of negative affectivity (NA) and one measuring levels of social inhibition (SI). Subjects who score a minimum of 10 points on both scales are indicated to have a Type D personality.

Physical activity and depression

Physical activity was assessed by one item. The nurse practitioner asked the patient how many hours per week they spend on 'active' physical activity (walking, cycling, stair climbing, gardening, etc., other than sports). Answer categories were 'never', '1-2 hours', '>2-4 hours', '>4-6 hours', and '>6 hours' per week. Physical activity was dichotomized with a cut-off point at 4 hours of physical activity per week.

Depressive symptoms were assessed using a validated Dutch version of the Edinburgh Depression Scale (EDS) (23-25). This is an 10-item self-rating scale in which each item is scored on a four-point Likert scale. Total scores can vary between 0 and 30 points, with a score of over 11 points indicating the presence of depression. Cut-off for depression was therefore set at an EDS score of 11 points.

Statistical analyses

Factor analysis and reliability analyses were performed to examine the internal validity and internal consistency of the DS14 in the type 2 diabetes population. T-test and chi-square statistics were used to indicate differences in demographics, depression, and lifestyle factors in individuals with and without a Type D personality. Single logistic regression analysis [odds ratios (ORs), 95% confidence intervals (CIs)] was used to assess the impact of the Type D personality on physical inactivity and depression. In the multiple logistic regression analysis, the impact of the Type D personality on depression and physical inactivity was adjusted separately for age, sex, smoking status, and alcohol intake (enter method). All variables were simultaneously entered in the multiple analysis. A value of $p< 0.05$ was considered to be statistically significant. All statistical analyses were performed using the SPSS version 14.0 for Windows.

RESULTS

Assessment of Type D personality

Internal validity of the negative affectivity and social inhibition items was determined by a factor analysis (n = 2556). Conforming the Type D personality model, two components were found (NA, eigenvalue = 6.15; SI, eigenvalue = 1.77) which explained 57% of the variance (see table 1). Factor loadings of the NA and SI items corresponded to their trait factor and ranged between .64 and .79 for NA items, and between .49 and .77 for SI items. Internal consistency was high, with a Cronbach's alpha of 0.87 for the NA scale and 0.83 for the SI scale, and corrected item total correlations ranging between 0.50 and 0.76 (NA), and between 0.35 and 0.69 (SI).

Table 1. Factor structure and internal consistency of the DS14 (n = 2556)

Items of the DS14	Factor analysis		Internal consistency**
	Factor I	Factor II	
Negative Affectivity			
(2) I often make a fuss about unimportant things	**0.64**		0.50
(4) I often feel unhappy	**0.74**	0.15	0.66
(5) I am often irritated	**0.74**	0.12	0.64
(7) I take a gloomy view of things	**0.78**	0.23	0.73
(9) I am often in a bad mood	**0.71**	0.25	0.65
(12) I often find myself worrying about something	**0.73**	0.19	0.68
(13) I am often down in the dumps	**0.79**	0.25	0.76
Eigenvalue I = 6.15			α = 0.87
Social Inhibition			
(1) I make contact easily when I meet people *		**-0.77**	0.55
(3) I often talk to strangers *	0.17	**-0.69**	0.35
(6) I often feel inhibited in social interactions	0.55	**0.49**	0.58
(8) I find it hard to start a conversation	0.39	**0.66**	0.66
(10) I am a closed kind of person	0.35	**0.63**	0.63
(11) I would rather keep other people at a distance	0.38	**0.63**	0.62
(14) When socializing, I don't find the right things to talk about	0.40	**0.67**	0.69
Eigenvalue II = 1.77			α = 0.83

* *Reversed keyed*

***Corrected item-total correlations*

Factor loadings are presented in ***bold***

Table 2 shows the characteristics of the respondents as a function of Type D personality. In all, 21% of the respondents had a Type D personality (n = 531). A significantly higher proportion of this group was female ($p < 0.0001$) and had a lower level of education ($p < 0.0001$) than the non-Type D group. Furthermore, significantly more non-Type D persons (5.9% vs. 3.6%) consumed more than 14 alcoholic beverages per week ($p = 0.037$). No differences were found in smoking status (14.3% vs. 12.1%, $p = 0.181$).

Table 2: Characteristics of respondents (n = 2556)

	Non-Type D personality (n = 2025)	Type D personality (n =531)	P value
	N (%)	N (%)	
Demographic features			
Female sex	979 (48.3)	305 (57.4)	P < 0.0001*
Age (mean, SD)	67.8 (10.1)	66.7 (11.0)	0.146
< 50	92 (4.5)	34 (6.4)	0.243
50-59	400 (19.8)	114 (21.5)	
60-69	669 (33.0)	172 (32.4)	
70-80	675 (33.3)	158 (29.8)	
> 80	189 (9.3)	53 (10.0)	
Educational level			P < 0.0001*
Low	1196 (59.1)	370 (69.8)	
Middle	531 (26.2)	101 (19.0)	
High	227 (11.2)	41 (7.8)	
Academic	71 (3.5)	19 (3.4)	
Marital status			0.109
With partner	1509 (74.5)	375 (70.6)	
Divorced	47 (2.3)	19 (3.6)	
Single	156 (7.7)	56 (10.5)	
Widow(er)	313 (15.5)	81 (15.3)	
Glycemic control			
HbA_{1c} (mean, SD)	6.7 (0.8)	6.7 (0.7)	0.094

** significant difference between groups (chi-square)*

*** significant difference between groups (t-test)*

Type D, physical inactivity, and depression

Figure 1 depicts the prevalence of physical inactivity and depression in Type D individuals and non-Type D individuals. With 56% of them performing a maximum of four hours of physical activity per week, individuals with a Type D personality were significantly less physically active than non-Type D individuals, of which 47% performed active physical activity for a maximum of four hours per week (unadjusted OR = 1.43, 95% CI 1.18 – 1.74, $p < 0.0001$). It was noteworthy that depression was much higher in Type D individuals (37%) than non-Type D individuals (7%) (unadjusted OR = 7.65, 95% CI 5.99 – 9.76, $p < 0.0001$).

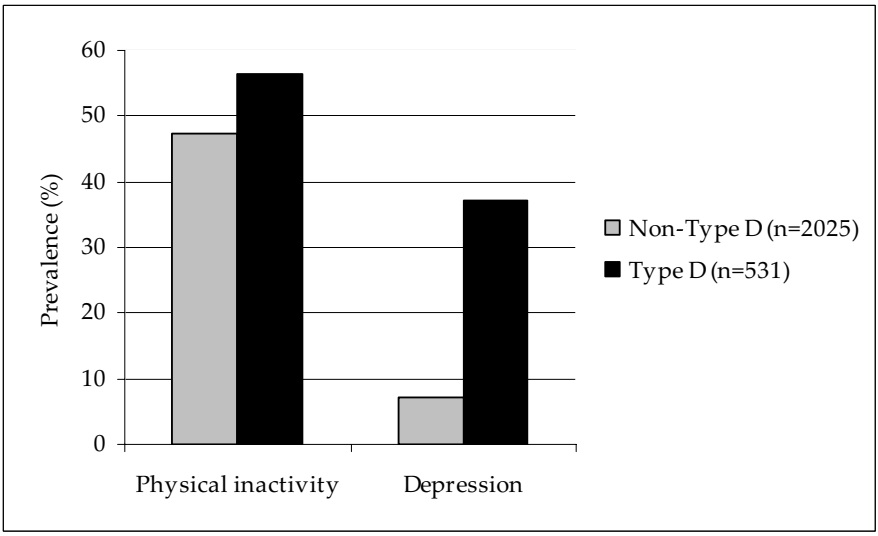

Figure 1: Prevalence of physical inactivity and depression in Type D versus non-Type D patients (n = 2556)

Multiple logistic regression analysis

Multiple logistic regression analyses were used to examine the independent effect of the Type D personality on both physical inactivity and depression, after adjustment for sex, age, smoking status, and alcohol intake (Table 3). These analyses indicated that the Type D personality was independently associated with an increased likelihood of physical inactivity (OR = 1.40). Other significant attributors to physical inactivity were female sex (OR = 1.50) and age (OR = 1.01). Type D personality was associated with a seven-fold increased likelihood of depression (OR = 7.41), after adjustment for other risk factors. Female sex (OR = 1.64), smoking (OR = 1.79), and alcohol intake (OR = 0.44) were other significant attributors to depression.

Table 3: Multiple logistic regression analyses

	Physical inactivity	P value	Depression	P value
	OR (95% CI)		OR (95% CI)	
Type D personality	**1.40** (1.15 – 1.70)	0.001	**7.41** (5.79 – 9.49)	< 0.0001
Female sex	**1.50** (1.28 – 1.76)	< 0.0001	**1.64** (1.27 – 2.12)	< 0.0001
Age	**1.01** (1.01 – 1.02)	0.001	1.01 (0.99 – 1.02)	0.399
Smoking	1.15 (0.90 – 1.46)	0.266	**1.79** (1.28 – 2.51)	0.001
Alcohol consumption (> 14 consumptions / week)	1.01 (0.71 – 1.44)	0.943	**0.44** (0.19 – 0.98)	0.044

Method: Enter
Significant odds ratio's are presented in ***bold***

DISCUSSION

This is the first study to investigate the Type D personality in individuals with type 2 diabetes, as well as the first study to examine the association between the Type D personality and physical inactivity. In line with previous research, female sex was a predictor for both depression (18; 19) and physical inactivity (5; 26). As expected, age was a factor related to physical inactivity (4; 5). Smoking status was associated only with depression, but not with physical inactivity. Type D individuals had a 1.4 likelihood of being physically inactive and a 7.4 likelihood of being depressed, compared with non-Type D individuals. Previous studies showed a similar association with depression (27). These findings suggest a potential role of the Type D personality in the context of diabetes. The assessment of the Type D personality with the DS14 showed a high level of internal validity and internal consistency in the present study. Hence, the DS14 may be an appropriate instrument to measure negative affectivity, social inhibition, and Type D personality in individuals with type 2 diabetes. The internal consistency of the NA and SI scales was comparable to previous validation studies of the DS14 in cardiac patients (12). A total of 21% of the respondents had a Type D personality, which is comparable to the prevalence found in the general population (12), but lower than that observed in populations with coronary heart disease (12; 28; 29).

Practical implications

In diabetes consultation, it may be useful to identify the Type D personality for two reasons. First, Type D individuals are at risk for clustering of psychosocial risk factors, such as depression, stress, and anxiety, which are also related to type 2 diabetes (30-32). Second, the presence of Type D personality may influence treatment by affecting the patient's perception and experience of diabetes and the patient's way of coping with the disease and its treatment. Type D individuals may experience the disease as being more disabling than non-Type D individuals, but they are less likely to express these symptoms and health concerns during consultation, which may hinder the patient-provider interaction (16). Both clustering of psychological risk factors (8; 33) and poor consultation behavior (16) may negatively influence the self-management performance and adherence to treatment. As a result, Type D individuals are less likely to respond well to treatment and are at risk for adverse health outcomes (16). It is therefore important to investigate whether careful and intensive monitoring of Type D individuals could help them to respond adequately to signs of psychosocial problems and may improve their self-management and adherence.

In the case of physical activity intervention, type 2 diabetes patients with a Type D personality may benefit from a more phased approach in which the individual has to gain confidence in his/her own abilities to exercise and become aware of the positive effects of physical activity before the physical activity is intensified. Thereby, regular feedback and support are of great importance to tackle possible barriers or negative experiences in Type D individuals.

Screening for the Type D personality may be useful since Type D is a broad and stable personality trait with great explanatory and predictive power (27), and is independently associated with a markedly increased risk of depressive symptoms. Curiously, though, the study of Fisher et al. (33), who assessed depression in type 2 diabetes patients, showed that most of the patients experiencing high levels of psychological distress were not clinically depressed. The authors stated that it may be more important to understand the impact of distress on poor behavioral disease management and its associated personal, disease-related, and social factors, rather than to identify depression. The DS14 is an easy-to-use assessment tool and therefore feasible in clinical practice. Hence, treatment interventions should be aimed at coping and problem-solving (33).

Strengths and limitations

This study has some limitations. First, non-responders and excluded patients might be more likely to have a Type D personality, which may limit the generalizability of the study outcomes. Second, due to the cross-sectional design of the study, no causal associations between the Type D personality and physical inactivity could be determined, nor could the possible

mediating role of depression in the association between the Type D personality and physical inactivity be studied. Third, physical activity was self-reported and scored in only one item. It encompassed a limited set of activities and did not include information about intensity, which may have led to an overestimation of physical activity. The strengths of this study are the large number of diabetes patients included, the study of psychological variables in the real world setting of diabetes care, and the standard assessment of the Type D personality.

Conclusions

In conclusion, the findings of this study show that having a Type D personality increases the likelihood of physical inactivity as well as depression in persons with type 2 diabetes. Since this is the first study to examine the Type D personality in individuals with type 2 diabetes, future studies should replicate our findings for a more accurate overview of the prevalence of Type D in this patient group. Furthermore, in examining the relationship between the Type D personality and physical inactivity, a longitudinal design should be applied. The presence of depression may be included as a possible mediator in this association. Finally, since Type D individuals score high on social inhibition, future research could focus on the role of social support in encouraging physical activity in these patients. The present findings suggest that it may be useful to screen patients for Type D personality in diabetes consultation to identify persons at risk for clustering of psychosocial risk factors, poor self-management, and unsuccessful treatment outcome. Diabetes patients with a Type D personality may need a more intensive approach and support in becoming physical active and staying that way, and in enhancing their emotional well-being.

REFERENCES

1. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
2. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C, White RD: Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 29:1433-1438, 2006
3. Hays LM, Clark DO: Correlates of physical activity in a sample of older adults with type 2 diabetes. Diabetes Care 22:706-712, 1999
4. Sherwood NE, Jeffery RW: The behavioral determinants of exercise: implications for physical activity interventions. Annu Rev Nutr 20:21-44, 2000
5. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W: Correlates of adults' participation in physical activity: review and update. Med Sci Sports Exerc 34:1996-2001, 2002
6. Goodwin RD: Association between physical activity and mental disorders among adults in the United States. Prev Med 36:698-703, 2003
7. Martinsen EW: Benefits of exercise for the treatment of depression. Sports Med 9:380-389, 1990
8. Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B: Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care 27:2154-2160, 2004
9. Rhodes RE, Smith NE: Personality correlates of physical activity: a review and meta-analysis. Br J Sports Med 40:958-965, 2006
10. Pedersen SS, van Domburg RT, Theuns DA, Jordaens L, Erdman RA: Type D personality is associated with increased anxiety and depressive symptoms in patients with an implantable cardioverter defibrillator and their partners. Psychosom Med 66:714-719, 2004
11. Black PH, Garbutt LD: Stress, inflammation and cardiovascular disease. J Psychosom Res 52:1-23, 2002
12. Denollet J: DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med 67:89-97, 2005
13. van den Broek KC, Martens EJ, Nyklicek I, van der Voort PH, Pedersen SS: Increased emotional distress in type-D cardiac patients without a partner. J Psychosom Res 63:41-49, 2007
14. Adler AI: Managing diabetes: what to do about cardiovascular disease. Diabetes Res Clin Pract 61 Suppl 1:S3-8, 2003
15. Diabetes mellitus: a major risk factor for cardiovascular disease. A joint editorial statement by the American Diabetes Association; The National Heart, Lung, and Blood Institute; The Juvenile Diabetes Foundation International; The National Institute of Diabetes and

Digestive and Kidney Diseases; and The American Heart Association. Circulation 100:1132-1133, 1999
16. Schiffer AA, Denollet J, Widdershoven JW, Hendriks EH, Smith OR: Failure to consult for symptoms of heart failure in patients with a type-D personality. Heart 93:814-818, 2007
17. Ketterer MW, Denollet J, Goldberg AD, McCullough PA, John S, Farha AJ, Clark V, Keteyian S, Chapp J, Thayer B, Deveshwar S: The big mush: psychometric measures are confounded and non-independent in their association with age at initial diagnosis of Ischaemic Coronary Heart Disease. J Cardiovasc Risk 9:41-48, 2002
18. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K: The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med 23:1165-1173, 2006
19. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 24:1069-1078, 2001
20. Katon WJ, Von Korff M, Lin EH, Simon G, Ludman E, Russo J, Ciechanowski P, Walker E, Bush T: The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. Arch Gen Psychiatry 61:1042-1049, 2004
21. AADE position statement. Individualization of diabetes self-management education. Diabetes Educ 33:45-49, 2007
22. Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, Blais MA, Meigs JB, Grant RW: Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. Diabetes Care 30:2222-2227, 2007
23. Cox JL, Chapman G, Murray D, Jones P: Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. J Affect Disord 39:185-189, 1996
24. Cox JL, Holden JM, Sagovsky R: Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 150:782-786, 1987
25. Pop VJ, Komproe IH, van Son MJ: Characteristics of the Edinburgh Post Natal Depression Scale in The Netherlands. J Affect Disord 26:105-110, 1992
26. Weyerer S: Physical inactivity and depression in the community. Evidence from the Upper Bavarian Field Study. Int J Sports Med 13:492-496, 1992
27. Denollet J: Type D personality. A potential risk factor refined. J Psychosom Res 49:255-266, 2000
28. Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL: Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet 347:417-421, 1996

29. Denollet J, Vaes J, Brutsaert DL: Inadequate response to treatment in coronary heart disease : adverse effects of type D personality and younger age on 5-year prognosis and quality of life. Circulation 102:630-635, 2000
30. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE: Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. Diabet Med 22:1379-1385, 2005
31. Steed L, Cooke D, Newman S: A systematic review of psychosocial outcomes following education, self-management and psychological interventions in diabetes mellitus. Patient Educ Couns 51:5-15, 2003
32. Delamater AM, Jacobson AM, Anderson B, Cox D, Fisher L, Lustman P, Rubin R, Wysocki T: Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. Diabetes Care 24:1286-1292, 2001
33. Fisher L, Skaff MM, Mullan JT, Arean P, Mohr D, Masharani U, Glasgow R, Laurencin G: Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. Diabetes Care 30:542-548, 2007

CHAPTER 6:

Type D personality and partner status in relation to physical inactivity and depression in patients with type 2 diabetes

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ABSTRACT

Objective: The aim of this study was to test whether Type D personality (tendency to experience emotional distress and inhibit expression of these emotions) and partner status have a synergistic effect on both physical inactivity and depression.

Research design and methods: 2556 primary care type 2 diabetes patients were stratified based on Type D personality, as assessed by the DS14 scale, and partner status, and group differences were examined according to demographics, physical inactivity, presence of depression, demographics, smoking status, and alcohol intake. Single and multiple logistic regression analyses (OR, 95% CI) were performed with physical inactivity as well as depression as the dependent variable and with the non-Type D respondents with a partner set as a reference group.

Results: In all, 21% of the individuals with type 2 diabetes had a Type D personality. Type D individuals without (OR = 2.04, 95% CI 1.44 – 2.88) and with a partner (OR = 1.35, 95% CI 1.08 – 1.70), and non-Type D individuals without a partner (OR = 1.30, 95% CI 1.05 – 1.60) had an increased likelihood for physical inactivity compared with non-Type D individuals with a partner, when corrected for sex, age, and lifestyle factors. Furthermore, Type D individuals with (OR = 6.52, 95% CI 4.82 – 8.78), and without a partner (OR = 11.70, 95% CI 7.96 – 17.18) had an increased likelihood of depression.

Conclusions: Having a Type D personality and being without a partner appeared to have a synergistic effect on both physical inactivity and depression.

INTRODUCTION

Type 2 diabetes is a complex chronic disease with high co-morbidity. Disease control aims at achieving and maintaining glycemic control, and reducing cardiovascular risk factors in order to prevent or delay vascular and neural complications. Glycemic control largely depends on lifestyle habits. Therefore, a major appeal is placed on diabetes patients' self-management capabilities (1), which has a great impact on the patients' daily life (2). One of the most important health behaviors in diabetes management is regular physical activity. Regular physical activity improves glycemic control and physical fitness is inversely related with morbidity and mortality in individuals with type 2 diabetes (3). Since it is such a major aspect of diabetes treatment, it may be useful to identify individuals at risk for poor lifestyle and poor self-management, and hence, poor health outcome. Understanding the determinants and underlying mechanisms of poor self-management behaviors may provide keys to intervention for patients at risk. These determinants consist of a complex interplay between social, mental and behavioral factors (4-6), which are often related to chronic diseases in general, like diabetes (4; 5; 7).

An example of these psychosocial factors is depression (4; 5; 8), which is significantly more prevalent in type 2 diabetes patients than in the general population (9). Depression is related to poor self-care behaviors, mortality, and increased health costs in individuals with type 2 diabetes (10).

In cardiovascular disease, a relatively new personality trait has also been studied which identifies patients who are prone to clustering psychological risk factors, such as depression (11). Subjects with this so called distressed or Type D personality have high levels of both negative affect (i.e. tendency to experience negative emotions across time and situations) (12), and social inhibition (i.e. tendency to inhibit expression of emotions and behaviors in social interactions to avoid disapproval) (13). This tendency to inhibit behavior in social interaction may hamper self-management, since it may be a barrier in health care provider - patient communication. Moreover, low self-esteem and a lack of motivation are common in people with type D personality, which may also be a barrier to improved diabetes management. However, in the scope of health and disease another factor may play a role, namely partner status. Several studies showed associations between having a partner and health status, and having a partner and lower mortality. For example, Manzoli et al. (2007) performed a meta-analysis on the effects of marital status on mortality, in a population of more than 250,000 elderly people. They found that marriage or support of a spouse significantly and independently reduced the risk of mortality with 9 to 15% (14). Furthermore, Schoenborn et al. (2004), showed in a U.S. population of 127,545 adults that married people scored better on nearly all health outcomes and health behaviors (15).

Two theories have been advocated to explain these associations. The marriage protection or social causation theory, proposes that marriage brings along some beneficial effects as in economic, psychological, and social support, whereas the marriage selection theory proposes that healthier individuals are more likely to marry and stay married, while less healthy people either never get married or are more likely to become divorced or widowed (14-16).
In previous research, social support consistently showed to be an important behavioral correlate of physical activity (17; 18). The spouse is one of the natural sources of social support in individuals (19). In line with the marriage protection theory, having a partner, if the relationship is satisfying, may have a protective effect on the negative influence of Type D on health outcomes, such as physical inactivity or depression (20). Therefore, the aim of this study was to test whether type D personality and being without a partner have a synergistic effect on both physical inactivity and depression in adults with type 2 diabetes mellitus.

RESEARCH DESIGN AND METHODS

Subjects

Between January and April 2006, in total 3300 individuals with type 2 diabetes, derived from 100 general practitioners in the Eindhoven region, the Netherlands were invited during their regular diabetes check-ups by their nurse practitioner to join an ongoing diabetes management project called 'DIAZOB'. Individuals in this cohort will be followed during their lifetime and will be periodically assessed for biological parameters and demographic, psychosocial, and lifestyle parameters in a patient survey. After exclusion of responders who gave no informed consent, and after excluding records due to missing data, 2556 participants were included in the final analysis (response rate after exclusion: 77%).

Clinical characteristics

Demographic variables included sex, age, marital status, and education level. The clinical characteristics included HbA_{1c} level (%), and the lifestyle factors included smoking status, and alcohol intake. All variables were patient-reported, except for HbA_{1c} values, which were measured at the Diagnostic Centre Eindhoven, the Netherlands, a primary care diagnostic institute.

Type D personality and partner status

Type D personality was assessed using the Type D Scale-14 (DS14) (11). This questionnaire consists of 14 items which are scored on a five-point Likert-scale ranging from 0 = 'false' to 4 = 'true'. The DS14 comprises two scales, one measuring levels of negative affectivity (NA) and one measuring levels of social inhibition (SI). Subjects who score a minimum of 10 points on both

scales are indicated to have a Type D personality. Previous findings showed adequate internal validity and internal consistency of the DS14, with a Cronbach 's alpha of 0.88 (NA) and 0.86 (SI), respectively (11). Current marital status was assessed by asking the respondent what applicable to them. Answer categories included: 'having a partner', 'being single', 'being divorced/separated', 'being widowed'. In the analyses, marital status was dichotomized as having a partner and having no partner.

Physical activity and depression

Physical activity was assessed during a nurse-led interview. The nurse practitioner asked the patient how many hours per week they spend on 'active' physical activity (walking, cycling, stair climbing, gardening, etcetera, other than sports). Answer categories were 'never', '1-2 hours', '>2-4 hours', '>4-6 hours', and '>6 hours' per week. Physical activity scores were dichotomized using a cut-off point at > 4 hours of physical activity per week. Depressive symptoms were assessed using the validated Dutch version of the Edinburgh Depression Scale (EDS) (21-23). This is a 10-item self-rating scale in which each item is scored on a four-point Likert-scale. Total scores can vary between 0 and 30 points, with a score of over 11 points indicating the presence of depression. In the present study, cut-off for depression was therefore set at an EDS score of more than 11 points.

Statistical analyses

Respondents were stratified based on Type D personality and partner status (with or without partner). Preliminary analysis (chi-square statistics) did not show any differences within the group without partner (including currently single, divorced, and widowed individuals) concerning prevalence of Type D (singles: 26%, divorced: 27%, widowed: 21%, p = 0.183), depression (singles: 18%, divorced: 24%, widowed:17%, p = 0.336), or physical inactivity (singles: 53%, divorced: 55%, widowed 57%, p = 0.655). ANOVA (continuous variables) and chi-square statistics (categorical variables) were used to indicate differences in demographics, HbA_{1c} levels, depression, and lifestyle factors between the four groups.
Chi-square statistics were used to detect difference in prevalence of physical inactivity and depression between non-Type D individuals with and without partner, and Type D individuals with and without partner. Single logistic regression analysis [odds ratios (ORs), 95% confidence intervals (CIs)] was used to assess the association between combined Type D personality and partner status, sex, age, smoking status, and alcohol use, respectively, and both dependent variables physical inactivity and depression. Those with a partner were used as the reference group. In the multiple logistic regression analysis the association between combined Type D personality and partner status and both depression and physical inactivity was adjusted separately

for age, sex, smoking status and alcohol intake (enter method). A value of $p< 0.05$ was considered to be statistically significant. All statistical analyses were performed using the SPSS version 14.0 for Windows.

RESULTS

Table 1 shows the characteristics of the respondents. Some 21% of the respondents had a Type D personality (n = 531). Furthermore, 26% of the respondents had no partner (n = 672). There were no significant differences between Type D and non-Type D individuals regarding partner status (29% versus 26% had no partner). Significant differences between groups were found for sex ($p < 0.0001$), with women being the most represented in the group Type D/no partner (70%). Individuals without a partner were significantly older than persons with a partner ($p <0.0001$). Furthermore, significant between - group differences were found in educational level ($p <0.0001$) with the Type D/no partner group having the lowest education level. The level of alcohol consumption was significantly higher in the non-Type D individuals with a partner, compared to the other groups. No significant between - group differences were found in HbA_{1c} levels, and smoking status (table 1).
Figure 1 shows the prevalence of physical inactivity and depression in all four groups stratified on Type D personality and partner status. Significant differences in physical activity were found between groups ($p < 0.0001$), with Type D individuals without a partner being the most physical inactive (65%). In addition, presence of depression was also significantly different between the groups ($p < 0.0001$), with individuals in the two Type D groups being more often depressed (with partner 33 %, without partner 48%, respectively) compared to the non-Type D individuals (with partner 7%, without partner 9%). Individuals without a partner had a significantly higher prevalence of physical inactivity (non-Type D: $p < 0.0001$, Type D: $p = 0.01$) compared to their counterparts with a partner, and Type D individuals without a partner had a significant higher prevalence of depression compared to Type D individuals with partner ($p = 0.001$).

Table 1: Characteristics (n = 2556)

	Non-Type D/partner (n = 1509) N (%)	Non-Type D/no partner (n = 516) N (%)	Type D/partner (n = 375) N (%)	Type D/no partner (n = 156) N (%)	P value
Demographic features					
Female sex	630 (41.7)	349 (67.6)	196 (52.3)	109 (69.9)	<0.0001*
Age (mean, sd)	66.0 (9.8)	72.3 (10.5)	65.6 (10.2)	69.9 (12.2)	<0.0001**
< 50	80 (5.3)	12 (2.3)	24 (6.4)	10 (6.4)	<0.0001*
50-59	335 (22.2)	65 (12.6)	90 (24.0)	24 (15.4)	
60-69	565 (37.4)	104 (20.2)	132 (35.2)	40 (25.6)	
70-80	461 (30.6)	214 (41.5)	109 (29.1)	49 (31.4)	
> 80	68 (4.5)	121 (23.4)	20 (5.3)	33 (21.2)	
Educational level					<0.0001*
Low	846 (56.2)	349 (67.5)	253 (67.5)	118 (76.0)	
Middle	418 (27.7)	112 (21.8)	77 (20.4)	24 (15.2)	
High	192 (12.7)	35 (6.8)	30 (8.0)	11 (7.2)	
Academic	53 (3.4)	20 (3.9)	15 (4.1)	3 (1.6)	
Glycemic control					
HbA_{1c} (mean, sd)	6.7 (0.8)	6.7 (0.7)	6.6 (0.6)	6.7 (0.8)	0.239
Lifestyle features					
Alcohol intake (>14 consumptions/week)	98 (6.5)	19 (3.7)	14 (3.7)	5 (3.2)	0.017*
Smoking	184 (12.2)	62 (12.0)	51 (13.6)	25 (16.0)	0.496

** significant difference between groups (chi square)*

*** significant difference between groups (ANOVA)*

Unadjusted analyses of the effect of Type D, and partner status separately, resulted in significantly increased likelihoods for both physical inactivity [OR = 1.43, 95% CI 1.18 – 1.74 (Type D), and OR = 1.53, 95% CI 1.28 – 1.82 (having no partner), respectively], and depression (OR = 7.65, 95% CI 5.99 – 9.76, and OR = 1.65, 95% CI 1.30 – 2.11,

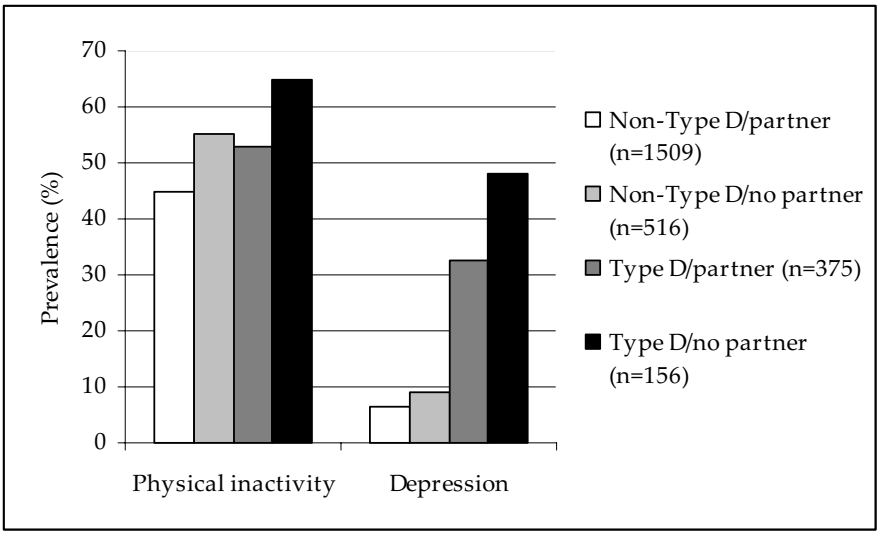

Figure 1: Prevalence of depression and physical inactivity in groups stratified by Type D and partner status

Table 2 shows the single logistic regression analyses including the combined Type D/partner status groups, with non-Type D individuals with a partner being the reference group. Subjects of the Type D/no partner group (OR = 2.28), the Type D/with partner group (OR 1.39), and the non-Type D/no partner group (OR = 1.53) were significantly more physically inactive than non-Type D individuals with a partner. Other significant attributors to physical inactivity were female sex (OR = 1.57), and higher age (OR = 1.01). Furthermore, Type D individuals with (OR = 6.78), and without a partner (OR = 13.19) were significantly more often depressed. Female sex (OR = 1.87), smoking (OR = 1.66), and alcohol intake (OR = 0.34) were also significantly associated with depression.

Table 2: Single logistic regression

	Physical inactivity	P-value	Depression	P-value
	OR (95% CI)		OR (95% CI)	
Non Type D/partner	1.00		1.00	
Non Type D/no partner	**1.53** (1.25 – 1.87)	<0.0001	1.39 (0.97 – 2.01)	0.074
Type D/partner	**1.39** (1.11 – 1.74)	0.005	**6.78** (5.10 – 9.24)	<0.0001
Type D/no partner	**2.28** (1.61 – 3.21)	<0.0001	**13.19** (9.07 – 19.18)	<0.0001
Female sex	**1.57** (1.35 – 1.84)	<0.0001	**1.87** (1.48 – 2.36)	<0.0001
Age	**1.01** (1.01 – 1.02)	<0.0001	1.00 (0.99 – 1.01)	0.647
Smoking	1.07 (0.84 – 1.35)	0.590	**1.66** (1.23 – 2.26)	0.001
Alcohol consumption (> 14 consumptions / week)	0.85 (0.61 – 1.21)	0.230	**0.34** (0.16 – 0.73)	0.006

Bold depicted Odds Ratios are significant

Multiple logistic regression analyses are shown in table 3, in which the combined effect of Type D and partner status on both physical inactivity and depression is accounted for sex, age, smoking status, and alcohol intake. Having a Type D personality and being with a partner (OR = 1.35), or without partner (OR = 2.04), and being non-Type D without a partner (OR = 1.30), and female sex (OR = 1.40) were significantly associated with physical inactivity. In addition, Type D patients with a partner (OR = 6.51), and without a partner (OR = 11.70) had a significantly increased likelihood for depression. Other factors significant related to depression were female sex (OR = 1.57), alcohol intake (OR = 0.43), and smoking (OR = 1.74).

Table 3: Multiple logistic regression

	Physical inactivity	P-value	Depression	P-value
	OR (95% CI)		OR (95% CI)	
Non Type D/partner	1.00		1.00	
Non Type D/no partner	**1.30** (1.05 – 1.60)	0.016	1.21 (0.83 – 1.77)	0.325
Type D/partner	**1.35** (1.08 – 1.70)	0.010	**6.51** (4.82 – 8.78)	<0.0001
Type D/no partner	**2.04** (1.44 – 2.89)	<0.0001	**11.70** (7.97 – 7.18)	<0.0001
Female sex	**1.39** (1.18 – 1.65)	<0.0001	**1.57** (1.21 – 2.03)	0.001
Age	1.01 (1.00 – 1.02)	0.054	1.00 (0.99 – 1.01)	0.76
Smoking	1.16 (0.92 – 1.48)	0.207	**1.75** (1.25 – 2.46)	0.001
Alcohol consumption (> 14 consumptions / week)	1.04 (0.72 – 1.49)	0.830	**0.43** (0.19 – 0.97)	0.042

Bold depicted Odds Ratios are significant
Method: Enter

DISCUSSION

This study tested whether Type D personality and being without a partner have synergistic effects on both physical inactivity and depression in individuals with type 2 diabetes mellitus. In all, 21% of the respondents had a Type D personality, and 26% had no partner. Being without a partner was, as may be expected in a sample of predominantly older adults, related to older age, and female sex. However, it was not related to Type D personality. No differences were found in prevalence of Type D personality, depression and physical inactivity within the group without a partner (single, divorced, widowed), which is in accordance with the findings of the meta-analysis of Manzoli et al. (2007) (14).

When comparing respondents based on stratification of Type D personality and partner status (being with or without partner), significant differences in the prevalence of physical inactivity and depression were found between Type D individuals and non-Type D individuals, and within both groups between individuals with and without a partner, except for the prevalence in depression within the two non-Type D groups.

Type D individuals without a partner had a twofold likelihood of being physically inactive compared to non-Type D individuals with a partner. The single effects of having a Type D personality and being without a partner were similar. The positive effect of having a partner on physical activity has also been found in several other studies (24-26). These studies showed that the exercise status of both partners was positively related. Furthermore, married people were not only more likely to participate in exercise, but had also higher levels of physical activity (including low intensity activities such as gardening, walking) (24). Both above mentioned effects yielded especially for married women. As consistently shown in previous research, female sex was negatively associated with physical activity (17; 18).

The association of older age with physical inactivity was washed out in the multivariate model, probably by the fact that widow(er)s are highly represented in this group. Type D individuals with and without a partner had respectively an eightfold and a fifteen fold risk to be depressed compared to non-Type D individuals with a partner, indicating that on top of the effect of having a Type D personality, being without a partner almost doubles the risk of being depressed. These rates are much higher than the ones found in a study of van den Broek et al. (2007), including a sample of cardiac patients, in which Type D patients with and without a partner had a fourfold and sevenfold risk, respectively of being depressed, compared to non-Type D's with a partner (20). Female sex (9; 27), and smoking status (28) were also associated with depression, which is in line with previous research.

Practical implications

When translating these findings into practice, it seems to be important to identify Type D individuals during diabetes consultation, especially those without a partner, since they may be highly at risk for depression as well as physical inactivity. These individuals may benefit from social support in performing lifestyle and self-management activities, in order to achieve positive health outcomes. However, in Type D individuals, social inhibition may lead to a small social network, and therewith decreased perceived social support (29). Herpetz et al. (2000), found that diabetes patients perceived their primary care provider as the most important source of psychosocial support second to their relatives (30). Therefore, diabetes care providers may be an important source of social support in adopting and maintaining healthy behaviors, such as physical activity. Furthermore, it may be useful for diabetes care providers to assess the social ties of Type D patients and try to involve them in self-management education and activities (4). In case of physical activity, Type D patients without a partner may benefit from supervised group exercise training. In this situation, the exercise trainer, and fellow group members (diabetes patients) may stimulate the Type D patient to become and maintain physical active. However, they may initially have to overcome the barrier of social interaction in a group situation.

Strengths and limitations

The strengths of this study are the large number of diabetes patients included, allowing for powerful subgroup analyses and the standardized and valid assessment of psychological variables, in a real world setting of diabetes care. This study has some limitations as well. First, non-responders and excluded patients might be more likely to have a Type D personality, which may limit the generalizability of the study outcomes. Second, due to the cross-sectional data, no causal associations between the Type D personality and physical inactivity could be determined. Third, physical activity was self-reported and scored in only one item. It encompassed a limited set of activities and did not include information about intensity, which may have led to an overestimation of physical activity. Fourth, only current marital status was assessed, while marital history may also influence health outcomes (15). Finally, no information was assessed on the quality of relationships, which is an important factor, since social ties may have both positive as well as negative effects on health (behavior) (31).

Conclusions

In conclusion, the findings of this study indicate a positive effect of having a partner with regard to depression and physical activity, especially in Type D individuals, who already have a greater likelihood for negative health outcome. This may be the result of social and economic support or selection, or a combination of both, and may be the result of better health behaviors found in married individuals (14). Future research should replicate our findings, since this is the first study to examine the combined effect of Type D personality and partner status on physical inactivity and depression. To further examine the combined effect of personality and partner status, a longitudinal design should be applied. Overall, the present findings suggest that in diabetes consultation, it may be important to identify Type D patients without a partner, and provide them social support in lifestyle and self-management activities.

REFERENCES

1. Snoek F, Visser A: Improving quality of life in diabetes: how effective is education? Patient Educ Couns 51:1-3, 2003
2. McKinlay J, Marceau L: US public health and the 21st century: diabetes mellitus. Lancet 356:757-761, 2000
3. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
4. AADE position statement. Individualization of diabetes self-management education. Diabetes Educ 33:45-49, 2007
5. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE: Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. Diabet Med 22:1379-1385, 2005
6. Jack L, Jr., Airhihenbuwa CO, Namageyo-Funa A, Owens MD, Vinicor F: The psychosocial aspects of diabetes care. Using collaborative care to manage older adults with diabetes. Geriatrics 59:26-31; quiz 32, 2004
7. Everson-Rose SA, Lewis TT: Psychosocial factors and cardiovascular diseases. Annu Rev Public Health 26:469-500, 2005
8. Delamater AM, Jacobson AM, Anderson B, Cox D, Fisher L, Lustman P, Rubin R, Wysocki T: Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. Diabetes Care 24:1286-1292, 2001
9. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 24:1069-1078, 2001
10. Piette JD, Richardson C, Valenstein M: Addressing the needs of patients with multiple chronic illnesses: the case of diabetes and depression. Am J Manag Care 10:152-162, 2004
11. Denollet J: DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med 67:89-97, 2005
12. Watson D, Pennebaker JW: Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychol Rev 96:234-254, 1989
13. Asendorpf JB: Social inhibition: a general– developmental perspective. In Emotion, Inhibition, and Health Traue HC, Pennebaker JW, Eds. Seattle, Hogrefe & Huber Publishers, 1993, p. 80-99
14. Manzoli L, Villari P, G MP, Boccia A: Marital status and mortality in the elderly: a systematic review and meta-analysis. Soc Sci Med 64:77-94, 2007
15. Schoenborn CA: Marital status and health: United States, 1999-2002. Adv Data:1-32, 2004
16. Waldron I, Hughes ME, Brooks TL: Marriage protection and marriage selection--prospective evidence for reciprocal effects of marital status and health. Soc Sci Med 43:113-123, 1996

17. Sherwood NE, Jeffery RW: The behavioral determinants of exercise: implications for physical activity interventions. Annu Rev Nutr 20:21-44, 2000
18. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W: Correlates of adults' participation in physical activity: review and update. Med Sci Sports Exerc 34:1996-2001, 2002
19. Rankin-Esquer LA, Deeter AK, Froelicher E, Barr Taylor C: Coronary Heart Disease:Intervention for Intimate Relationship Issues. Cognitive and Behavioral Practice 7:212-220, 2000
20. van den Broek KC, Martens EJ, Nyklicek I, van der Voort PH, Pedersen SS: Increased emotional distress in type-D cardiac patients without a partner. J Psychosom Res 63:41-49, 2007
21. Cox JL, Chapman G, Murray D, Jones P: Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. J Affect Disord 39:185-189, 1996
22. Cox JL, Holden JM, Sagovsky R: Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 150:782-786, 1987
23. Pop VJ, Komproe IH, van Son MJ: Characteristics of the Edinburgh Post Natal Depression Scale in The Netherlands. J Affect Disord 26:105-110, 1992
24. Pettee KK, Brach JS, Kriska AM, Boudreau R, Richardson CR, Colbert LH, Satterfield S, Visser M, Harris TB, Ayonayon HN, Newman AB: Influence of marital status on physical activity levels among older adults. Med Sci Sports Exerc 38:541-546, 2006
25. Satariano WA, Haight TJ, Tager IB: Living arrangements and participation in leisure-time physical activities in an older population. J Aging Health 14:427-451, 2002
26. Schone BS, Weinick RM: Health-related behaviors and the benefits of marriage for elderly persons. Gerontologist 38:618-627, 1998
27. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K: The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med 23:1165-1173, 2006
28. Husky MM, Mazure CM, Paliwal P, McKee SA: Gender differences in the comorbidity of smoking behavior and major depression. Drug Alcohol Depend 93:176-179, 2008
29. Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL: Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet 347:417-421, 1996
30. Herpetz S, Johann B, Lichtblau K, al. e: [Patients with diabetes mellitus:Psychosocial stress and use of psychosocial support: A multicenter study.]. Med Klim 95:369-377, 2000
31. van Dam HA, van der Horst FG, Knoops L, Ryckman RM, Crebolder HF, van den Borne BH: Social support in diabetes: a systematic review of controlled intervention studies. Patient Educ Couns 59:1-12, 2005

CHAPTER 7:

General discussion

Physical activity is one of the key strategies in the prevention and delay of complications in diabetes management. Although there is a large body of evidence available about the benefits of physical activity it is still underutilized in diabetes care (1; 2). In addition, the prevalence of physical inactivity in patients with type 2 diabetes is high. In order to counteract physical inactivity in patients with type 2 diabetes, it is timely to study its determinants. The present thesis was therefore aimed to identify factors related to physical inactivity, thereby investigating a set of psychosocial factors.

BENEFITS OF PHYSICAL ACTIVITY IN DIABETES MANAGEMENT

Some of the findings of the meta-analysis on the effects of structured exercise interventions on diabetes outcomes indicate clinical significant risk reduction of complications and mortality. The effects of the two aerobic exercise modalities on HbA_{1c}, concurred with that of intensive medical treatment (3). Findings of the UK Prospective Diabetes Study (UKPDS) have shown that reductions in HbA_{1c} and blood pressure as obtained by the two aerobic exercise modalities (HbA_{1c}), and the combined exercise modality (blood pressure), respectively, induce significant risk reduction in all diabetes-related end points (4). Additionally, the effects of aerobic exercise on VO_2-max accounts for important risk reduction in overall mortality (5). In the meta-analysis, none of the three modalities clearly excelled. The interventions included in the meta-analysis required high levels of supervision and specific equipment, and were performed in small groups of probably highly motivated individuals. Information about the long term adherence to these interventions is scarce. The feasibility for real-world settings can therefore be questioned.

PSYCHOSOCIAL FACTORS IN THE DIAZOB STUDY

The cohort (n = 3300) of patients with type 2 diabetes as described in this thesis is a predominantly Caucasian, non-urban population, with a mean age of 67.7 ± 10.5 years and roughly equal sex distribution. Level of education was generally low, and the majority of people lived with a partner. The mean HbA_{1c} of the participants was 6.7 ± 0.7%, the mean BMI was 29.6 ± 4.6, and 14.9% of the participants smoked.

Depression in patients with type 2 diabetes

The prevalence of depression in insulin-naïve patients with type 2 diabetes (n = 1269) was 11%, which was lower compared to the rates found in community and primary care samples in Dutch studies (ranging from 17% to 29%) (6-9) as well as international studies (pooled mean 17%) (10). One of the

most important factors in the etiology of depression in patients with diabetes may be the presence of diabetes related complications. However, insulin-naïve patients with vascular co morbidities were not more depressed compared to those without vascular co-morbidities. Nonetheless, the multiple regression analyses showed that having two or more vascular co-morbidities approximately doubled the likelihood of depression compared to having diabetes only. Analyses for each specific vascular co-morbidity separately showed that this increased likelihood of depression yielded for almost all vascular co-morbidities in combination with coexisting vascular co morbidities, but especially for the presence of coronary heart disease and neuropathic foot. Noticeably, no relationship was found between levels of HbA_{1c} and depression, which is in contrast with the findings of a recent meta-analysis (11). This might be due to the relative well managed glycemic control of the relatively uncomplicated insulin-naïve primary care sample, although others did not find a relationship either. (7; 12; 13). In two of these studies, rates and odds of depression were significantly increased in individuals with diagnosed type 2 diabetes compared to non-diabetic subjects, but not in individuals with undiagnosed type 2 diabetes (7; 13). This may indicate that the increased prevalence of depression in patients with type 2 diabetes may be related to the burden of the disease reflected by presence of co-morbidities and the awareness of having a serious disease. Conversely, presence of depression may also increase the risk of poor health outcome in patients with type 2 diabetes. Black et al. (2003), performed a prospective, longitudinal study over a time span of five years, in older adults with type 2 diabetes. They found that presence of depression was an important predictor of greater incidence of both disability in activities of daily living and vascular complications, as well as greater mortality (14).

Type D personality in patients with type 2 diabetes

Distressed or Type D patients score high on both negative affectivity (i.e. the tendency to experience negative emotions across time and situations) and social inhibition (i.e. the tendency to inhibit expression of emotions and behaviors in social interactions to avoid disapproval) (15). They have a predisposition for clustering psychological factors, such as depression, and for adverse health outcome. Furthermore, the accompanying social inhibition may often be related to experiences of social alienation (16). About twenty-one percent of the patients in the cohort had a Type D personality. This proportion was comparable to the prevalence shown in the general population, but was lower than the prevalence found in populations with cardiovascular diseases (17).

Relationship between Type D and depression

Patients with a Type D personality had a sevenfold likelihood to experience depressive symptoms compared to non-Type D patients. When closely studying depression within Type D patients stratified by partner status, Type D patients without a partner even had a thirteen fold risk to experience depressive symptoms compared to non-Type D patients with a partner. These results indicate a possible protective effect of having a partner, therewith to some extent counteracting the negative impact of Type D personality. In chapter 3, low levels of social support were also related to depression, although this relationship may be bi-directional. The results of the study in chapter 6, however, show that social support may be particularly important for mental health in individuals with a Type D personality, since prevalence of depression did not differ between non-Type D individuals with and without a partner.

PHYSICAL INACTIVITY AND ITS RELATED FACTORS IN THE DIAZOB STUDY

About 48% of patients in the cohort (43% of the males, 53% of the females) were physically inactive (e.g. performed less than four hours of 'active' physical activities per week). Similar to findings in the general population, physical inactivity was related to older age, being female, being without a partner and having a high BMI. Participants who experienced depressive symptoms had a 1.7 fold likelihood of physical inactivity, which corresponds with the results of previous studies in patients with type 2 diabetes (18; 19), and in the general population (20). Various characteristics of depression such as lack of motivation, low self-esteem, having difficulty with problem-solving and feelings of helplessness and hopelessness, together with the withdrawal from social contacts, make it difficult to initiate, adopt to and maintain physical activity (20). Vickers et al. (2006) showed that especially individuals with higher levels of depressive symptoms are less likely to use relapse prevention behaviors, which makes them to give up easily(21). Patients with a Type D personality had a 1.4 fold likelihood for physical inactivity. When specified to partner status, Type D patients with a partner had a 1.3 likelihood of being physically inactive compared to non-Type D patients with a partner. This likelihood was similar to that of non-Type D patients without a partner. Type D patients without a partner, however, had a twofold likelihood for physical inactivity. Again, being with a partner showed to have some protective effect, only now in Type D patients as well in non-Type D patients. Both studies, as described in chapter 5 and 6, add to the hypothesis that Type D personality may partly affect health outcome indirectly by influencing health-related behaviors (physical activity), and social support (16). In their study, Williams et al. showed in a population of

healthy young adults that Type D individuals were less likely to engage in health-related behaviors compared to non-Type D individuals. Furthermore, Type D individuals reported lower levels of social support. Noticeably, both findings remained significant after controlling for neuroticism. This stresses the crucial combination of negative affect and social inhibition in the Type D construct which often has been criticized as being just a synonym of neuroticism (16). Additionally, Steptoe and Molloy (2007), already suggested the importance of understanding the role of social context in defining the influence of personality on health outcome (22).

MULTIPLE RISK ASSESSMENT IN DIABETES MANAGEMENT

Currently, diabetes management has a predominantly biomedical basis, focusing on controlling biological factors such as HbA_{1c}, blood pressure and lipid profile. Overlooking the DIAZOB cohort as described in the present thesis, it can be concluded that diabetes management in Dutch primary care is quite effective in obtaining good glycemic control. On the other hand, the management of lifestyle factors (physical activity, overweight, and smoking) was relatively poor, as shown in of diabetes programs in both the Netherlands and abroad (23). Furthermore, Dutch diabetes care standards do not address to psychosocial factors, and for example depression is poorly recognized and treated in patients with diabetes (24). However, focusing on biophysiological, as well as psychosocial and behavioral processes of disease and their interrelationship, may lead to better understanding of the determinants and pathways of disease (25). Hence, when more attention is paid to lifestyle behaviors such as physical activity, and psychosocial factors in diabetes management, a considerable amount of morbidity, disability and mortality may be prevented (26).

Multiple risk assessment is a useful tool to apply the knowledge of the determinants of disease. Multiple risk assessment has several purposes in clinical practice (27). First, high-risk patients who need further assessment and/or specific attention and intervention can be identified. For example, the results of the present thesis showed that individuals with a Type D personality, a depression, or without a partner are more likely to be physical inactive. These psychosocial factors may be barriers to initiate and maintain physical activity. Furthermore, several psychosocial factors are also associated with inadequate health care utilization (28). Secondly, with this in mind efforts needed for risk-reduction intervention, such as physical activity, can be modified based on the risk profile. Third, physical activity interventions should be developed targeting specific groups and tailored to the needs of these groups.

The setting of primary diabetes care provides an important opportunity to assess and address to multiple health risk factors (29). Physical activity, depression, Type D personality and social support, can be easily assessed by short, validated self-report questionnaires, making it feasible to use in primary diabetes care. Signs of depression and distress thereby may be easily detected, while these detection rates are currently low (24). The questionnaires may be preferably filled in and scored prior to clinical visit, saving time during consultation and making it possible to directly address the results (26). The use of self-report questionnaires requires no extensive training of the health care professionals involved, which increases the chance of successful integration in routine care. Finally, multiple risk assessment gives health care providers a clear starting point to provide their patients information about their disease and its attributes and consequences, which may help motivating patients to adjust and adhere to subsequent intervention (27).

In addition, the longitudinal nature of primary care provides a venue to promote physical activity and to provide assistance with making lifestyle changes for a long period of time (30). The patients treated in primary care have relatively uncomplicated diabetes and are diagnosed at an increasing earlier age. Therefore, cardiovascular risk reduction in this group may eventually induce large benefits in health and health-related costs. Physical activity promotion may be initiated shortly after diagnosis, since the realization of a life long chronic disease has just set in, and potential impact of the prevention program might be largest. Physical activity is pre-eminently an intervention that fits in a biopsychosocial approach of disease since it addresses physical as well as emotional health (31). However, it may be suggested that another approach to physical activity in diabetes care is needed. In stead of developing interventions aiming at achieving the most optimal (biological) effects on diabetes, as the exercise interventions described in the meta-analysis, more effort should be put in studies aiming at developing effective strategies to initiate and maintain physical activity in patients with type 2 diabetes, since these are currently limited (32).

CONCLUDING SUMMARY

In sum, the present thesis showed that physical activity is an important modality in the prevention or delay of cardiovascular complications. Furthermore, information was provided about the prevalence of depression in Dutch, mainly Caucasian, patients with type 2 diabetes which was hardly available, as well about the prevalence of Type D personality which was previously unknown. It was shown that these psychosocial factors may play an important role in physical inactivity in patients with type 2 diabetes, and therefore in the process of initiating and maintaining a physical active lifestyle as well.

This indicates that diabetes management calls for a biopsychosocial approach. Broadening diabetes management by including proper attention to lifestyle behaviors such as physical activity and to psychosocial factors, in terms of assessment, support and intervention, may prevent considerable amount of morbidity, disability and mortality. Additionally, in counteracting physical inactivity, interventions may therefore aim at initiating and maintaining physical activity and should target specific risk groups and be tailored to their needs.

STRENGTHS AND LIMITATIONS OF THE THESIS

This thesis has several strengths. First, the large study sample, which allows for powerful subgroup analyses. Second, the composition of the cohort. The patients with type 2 diabetes of 100 general practitioners, were asked to join the study during regular diabetes check up based on solely the criteria of being able to fill in the questionnaire. Therefore, the cohort that was assembled can be regarded to adequately represent the primary care setting, in which 80-90% of diabetes management takes place. Assessments, and especially of psychosocial factors, in the real-world setting of primary care are important, since these are often performed in selective populations e.g. from secondary care. Third, the broad range of variables assessed and used in the analyses provides extensive information of the relative contribution of demographics, psychosocial factors and lifestyle variables to physical inactivity as well as to depression in patients with type 2 diabetes.

The findings presented in this thesis have to be interpreted with some caution given the cross-sectional design of the studies, which does not allow for making inferences about causality or mediation. However, presence of a strong association, of which many were found in this baseline assessment, is a prerequisite to examine causality. Another limitation concerns the assessment tools as applied in the present thesis. Physical activity was self-reported and scored by only one item. It encompassed a limited set of activities and did not include information about intensity. This, together with possible effects of social desirability and retrospection biases may have led to an overestimation of physical activity. Furthermore, presence of depression can only be assessed by a structured clinical interview. In stead, depressive symptoms were assessed by a self-reported EDS scale. However, given the scope of the study design in which a large cohort is followed periodically for years, it would be impossible to perform these interviews. Generalizability of the study outcomes may be limited to a predominantly Caucasian non-urban population. Finally, non-responders and excluded patients (about 20% of the total sample) might be more likely to have a Type D personality, or to be depressed, which may also limit the generalizability of the study outcomes.

RECOMMENDATIONS

Based on this thesis, several recommendations can be made for research purposes, as well as for clinical practice.

Recommendations for future research

Recommendations for future research are as follows:

1 To obtain more in-depth knowledge of the role that psychosocial factors may play in physical inactivity in patients with type 2 diabetes, the cross-sectional findings of this thesis should be replicated using a longitudinal design in order to provide information about the nature and the direction of the associations found.
2 Studies with a longitudinal design and long term follow-up should be performed to further decipher the interrelationships between psychosocial factors (depression, Type D personality, social support), lifestyle behaviors such as physical activity, and biophysiological factors (e.g. glycemic control, blood pressure, lipid profile, macro- and microvascular complications, and mortality), in order to understand the pathways of disease in type 2 diabetes.
3 A range of interventions for the promotion of physical activity in patients with type 2 diabetes in primary care should be developed and evaluated, thereby investigating which approach is most effective for the promotion of physical activity in certain subgroups of physically inactive individuals.
4 These interventions should be tested in randomized controlled trials including, next to biological outcomes, adherence and psychosocial factors as outcome measures and with a duration of at least one year to investigate long term effects.

Recommendations for clinical practice

Recommendations for clinical practice are as follows:

1 Diabetes management requires a biopsychosocial approach. Currently, it is too much focused on biomedical aspects, and psychosocial factors are less well addressed.
2 Since physical inactivity is high in patients with type 2 diabetes, and physical activity has important physical as well as emotional benefits, more attention has to be paid to physical activity in diabetes management.
3 Multiple risk assessment including psychosocial factors (depression, Type D personality and social support) and physical activity next to biophysiological factors should become part of quality of care as indicated in national diabetes care standards, and should be integrated in routine diabetes care.
4 Multiple risk assessment should be performed at least once a year.
5 To be able to sufficiently address to psychosocial factors related to diabetes and it management, a psychologist should be part of the multidisciplinary diabetes team in primary care.

REFERENCES

1. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, Verity LS: American College of Sports Medicine position stand. Exercise and type 2 diabetes. Med Sci Sports Exerc 32:1345-1360, 2000
2. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW: Are health care professionals advising patients with diabetes or at risk for developing diabetes to exercise more? Diabetes Care 29:543-548, 2006
3. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ: Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. Jama 286:1218-1227, 2001
4. Stratton IM, Cull CA, Adler AI, Matthews DR, Neil HA, Holman RR: Additive effects of glycaemia and blood pressure exposure on risk of complications in type 2 diabetes: a prospective observational study (UKPDS 75). Diabetologia 49:1761-1769, 2006
5. Blair SN, Kohl HW, 3rd, Barlow CE, Paffenbarger RS, Jr., Gibbons LW, Macera CA: Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. Jama 273:1093-1098, 1995
6. Bierman E, Comijs H, Depla M, ten Have M, Pot A: Psychische problemen en GGZ-gebruik bij ouderen met lichamelijke aandoeningen. Monitor Geestelijke Gezondheidszorg Ouderen. Rapportage 2006 Abstract. Utrecht, Trimbos-instituut, 2007
7. Knol MJ, Heerdink ER, Egberts AC, Geerlings MI, Gorter KJ, Numans ME, Grobbee DE, Klungel OH, Burger H: Depressive symptoms in subjects with diagnosed and undiagnosed type 2 diabetes. Psychosom Med 69:300-305, 2007
8. Pouwer F, Beekman AT, Nijpels G, Dekker JM, Snoek FJ, Kostense PJ, Heine RJ, Deeg DJ: Rates and risks for co-morbid depression in patients with Type 2 diabetes mellitus: results from a community-based study. Diabetologia 46:892-898, 2003
9. van Meeteren-Schram M, Baan C: Diabetes en depressie, een zorgelijk samenspel. Bilthoven, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), 2007
10. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K: The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med 23:1165-1173, 2006
11. Lustman PJ, Clouse RE: Depression in diabetic patients: the relationship between mood and glycemic control. J Diabetes Complications 19:113-122, 2005
12. Georgiades A, Zucker N, Friedman KE, Mosunic CJ, Applegate K, Lane JD, Feinglos MN, Surwit RS: Changes in depressive symptoms and glycemic control in diabetes mellitus. Psychosom Med 69:235-241, 2007

13. Palinkas LA, Barrett-Connor E, Wingard DL: Type 2 diabetes and depressive symptoms in older adults: a population-based study. Diabet Med 8:532-539, 1991
14. Black SA, Markides KS, Ray LA: Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. Diabetes Care 26:2822-2828, 2003
15. Denollet J: DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med 67:89-97, 2005
16. Williams L, O'Connor RC, Howard S, Hughes BM, Johnston DW, Hay JL, O'Connor DB, Lewis CA, Ferguson E, Sheehy N, Grealy MA, O'Carroll RE: Type-D personality mechanisms of effect: the role of health-related behavior and social support. J Psychosom Res 64:63-69, 2008
17. van den Broek KC, Martens EJ, Nyklicek I, van der Voort PH, Pedersen SS: Increased emotional distress in type-D cardiac patients without a partner. J Psychosom Res 63:41-49, 2007
18. Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B: Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care 27:2154-2160, 2004
19. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW: Physical activity in U.S. adults with diabetes and at risk for developing diabetes, 2003. Diabetes Care 30:203-209, 2007
20. Seime RJ, Vickers KS: The challenges of treating depression with exercise: from evidence to practice. Clin Psychol Sci Prac 13:194-197, 2006
21. Vickers KS, Nies MA, Patten CA, Dierkhising R, Smith SA: Patients with diabetes and depression may need additional support for exercise. Am J Health Behav 30:353-362, 2006
22. Steptoe A, Molloy GJ: Personality and heart disease. Heart 93:783-784, 2007
23. Welschen LM, van Oppen P, Dekker JM, Bouter LM, Stalman WA, Nijpels G: The effectiveness of adding cognitive behavioural therapy aimed at changing lifestyle to managed diabetes care for patients with type 2 diabetes: design of a randomised controlled trial. BMC Public Health 7:74, 2007
24. Pouwer F, Beekman AT, Lubach C, Snoek FJ: Nurses' recognition and registration of depression, anxiety and diabetes-specific emotional problems in outpatients with diabetes mellitus. Patient Educ Couns 60:235-240, 2006
25. Lindau ST, Laumann EO, Levinson W, Waite LJ: Synthesis of scientific disciplines in pursuit of health: the Interactive Biopsychosocial Model. Perspect Biol Med 46:S74-86, 2003
26. Babor TF, Sciamanna CN, Pronk NP: Assessing multiple risk behaviors in primary care. Screening issues and related concepts. Am J Prev Med 27:42-53, 2004

27. Grundy SM, Pasternak R, Greenland P, Smith S, Jr., Fuster V: Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. Circulation 100:1481-1492, 1999
28. Albus C, Jordan J, Herrmann-Lingen C: Screening for psychosocial risk factors in patients with coronary heart disease-recommendations for clinical practice. Eur J Cardiovasc Prev Rehabil 11:75-79, 2004
29. Coups EJ, Gaba A, Orleans CT: Physician screening for multiple behavioral health risk factors. Am J Prev Med 27:34-41, 2004
30. Goldstein MG, Whitlock EP, DePue J: Multiple behavioral risk factor interventions in primary care. Summary of research evidence. Am J Prev Med 27:61-79, 2004
31. Smith TW, MacKenzie J: Personality and risk of physical illness. Annu Rev Clin Psychol 2:435-467, 2006
32. Kirk AF, Barnett J, Mutrie N: Physical activity consultation for people with Type 2 diabetes: evidence and guidelines. Diabet Med 24:809-816, 2007

Summary

Samenvatting

SUMMARY

Currently, the growth of diabetes takes on epidemic proportions, which will even grow faster in the next years. Therewith, an increasing number of patients with diabetes will develop complications, which greatly impacts quality of life of the individual involved, as well as health care use and related costs. This development will be strengthened by the fact that type 2 diabetes, the most common type of diabetes, sets on at an increasing earlier age, which will increase the likelihood of complications over time as well. Effective treatment strategies to prevent or delay complications are therefore more than ever needed. Physical inactivity is one of the most important causes of type 2 diabetes. Conversely, physical activity has been proven to be an effective strategy in diabetes management. However, prevalence of physical inactivity is high in patients with type 2 diabetes. Psychosocial factors may play an important role in physical inactivity, since they affect health behavior in general. Therefore, the general aim of the current thesis was to study possible factors related to physical inactivity in patients with type 2 diabetes, with an emphasis on psychosocial factors.

The meta-analysis described in Chapter 2, showed some small to moderate effects of structured exercise interventions on HbA_{1c}, blood pressure, and maximum exercise capacity (VO_2-max), which may induce clinically significant cardiovascular risk reduction. Chapter 3 included a study of depression in insulin-naïve diabetes patients. Previous research showed an increased prevalence of depression in patients with type 2 diabetes, which may be partly explained by the presence of complications. The study in Chapter 3 showed a relatively low prevalence of depression in insulin-naïve diabetes patients. Furthermore, rates of depression did not differ between those with and without vascular co-morbidities. Multiple regression analyses showed, however, that having two or more vascular co-morbidities, and in particular coronary heart disease or neuropathic foot with co-existing co-morbidities, increased the odds of depression.

The study presented in Chapter 4 showed that depression was associated with physical inactivity in patients with type 2 diabetes. Furthermore, physical inactivity was related to higher age, female sex, being without partner, and having a high BMI. Chapter 5 included a study of Type D personality in patients with type 2 diabetes. Prevalence of Type D personality in the current cohort was similar to rates reported in the general population. Individuals with a Type D personality had an increased likelihood of physical inactivity as well as depression. Additionally, in the study as described in Chapter 6, it was tested whether a Type D personality and being without a partner have a synergistic effect on both physical inactivity and depression in adults with type 2 diabetes. It was shown that Type D individuals without a partner had an increased likelihood of both depression and physical inactivity, compared to non-Type D individuals with a partner.

In Chapter 7, the main outcomes of the current thesis were discussed, and recommendations for future research and clinical practice were given. It was shown that psychosocial factors are important factors related to physical activity in patients with type 2 diabetes. Therefore, diabetes management requires a biopsychosocial approach. Multiple risk assessment including psychosocial as well as biophysiological factors should be integrated in care routine. Studies should be performed investigating how to initiate and maintain physical activity. Finally, physical activity interventions should target specific risk groups and be tailored to their specific needs.

SAMENVATTING

De prevalentie van diabetes heeft vandaag de dag epidemische vormen aangenomen en zal de komende jaren sterk stijgen. Hierdoor zal een toenemend aantal patiënten met diabetes complicaties gaan ontwikkelen, die op hun beurt weer een grote impact hebben op zowel de kwaliteit van leven als het gebruik van gezondheidszorg en aanverwante kosten. Deze ontwikkeling zal nog eens worden versterkt door het feit dat type 2 diabetes, de meest voorkomende vorm van diabetes, op een steeds jongere leeftijd aanvangt, waardoor de kans op complicaties alleen maar vergroot wordt. De noodzaak voor effectieve behandelingsstrategieën ter preventie of uitstel van complicaties is daarom groot. Lichamelijke inactiviteit is één van de belangrijkste oorzaken van type 2 diabetes. Omgekeerd is lichamelijke activiteit een bewezen effectieve strategie in de behandeling van diabetes. Echter, de prevalentie van lichamelijke inactiviteit onder patiënten met type 2 diabetes is hoog. Psychosociale factoren spelen mogelijk een belangrijke rol in lichamelijke activiteit aangezien deze gezondheidsgedrag in het algemeen beïnvloeden. Het belangrijkste doel van dit proefschrift was daarom om factoren te bestuderen die mogelijk gerelateerd zijn aan lichamelijke inactiviteit bij patiënten met type 2 diabetes, daarbij de nadruk leggend op psychosociale factoren.

De meta-analyse, zoals beschreven in Hoofdstuk 2, liet zien dat gestructureerde bewegingsinterventies geringe tot matige effecten bewerkstelligden op HbA_{1c}, bloeddruk en maximale inspanningscapaciteit (VO_2-max), welke gerelateerd zijn aan significante verlaging van het cardiovasculair risico. Hoofdstuk 3 bevatte een studie van depressie in insuline-naïeve diabetes patiënten. Eerder onderzoek heeft uitgewezen dat de prevalentie van depressie is verhoogd in patiënten met type 2 diabetes, wat mogelijk gedeeltelijk verklaard kan worden door de aanwezigheid van complicaties. De studie in Hoofdstuk 3 liet een relatief lage prevalentie van depressie zien in insuline-naïeve diabetes patiënten. Ook werd er geen verschil gevonden in de prevalentie van depressie tussen patiënten met en zonder vasculaire comorbiditeiten. Meervoudige regressie analyse liet echter zien dat het hebben van twee of meer vasculaire comorbiditeiten, en in het bijzonder coronaire hart ziekte of neuropatische voet in combinatie met andere vasculaire comorbiditeiten, de kans op depressie vergrootte.

De studie die gepresenteerd werd in Hoofdstuk 4 liet zien dat depressie was geassocieerd met lichamelijke inactiviteit in patiënten met type 2 diabetes. Daarnaast was lichamelijke inactiviteit gerelateerd aan hogere leeftijd, vrouwelijk geslacht, geen partner hebben en het hebben van een hoog BMI. Hoofdstuk 5 bevatte een studie van Type D persoonlijkheid in patiënten met type 2 diabetes. De prevalentie van Type D persoonlijkheid in het cohort kwam overeen met de prevalentie zoals gerapporteerd in de algemene

populatie. Mensen met een Type D persoonlijkheid hadden een verhoogde kans op zowel lichamelijke inactiviteit als depressie. Aansluitend werd in de studie zoals beschreven in Hoofdstuk 6 getest of de combinatie van een Type D persoonlijkheid en alleenstaand zijn een synergistisch effect zou hebben op zowel lichamelijke inactiviteit als depressie. Personen met Type D zonder partner bleken een verhoogde kans op zowel depressie als lichamelijke inactiviteit te hebben vergeleken met personen zonder Type met partner. In Hoofdstuk 7 werden de belangrijkste uitkomsten van dit proefschrift besproken en aanbevelingen gedaan voor toekomstig onderzoek en de klinische praktijk. De behandeling van diabetes vraagt om een biopsychosociale benadering. Het is gebleken dat psychosociale factoren gerelateerd zijn aan lichamelijke activiteit bij patiënten met type 2 diabetes. Het is van belang dat meervoudige risicobepaling met daarin zowel psychosociale als biofysiologische factoren geïntegreerd wordt in de behandelingsroutine. Daarnaast zouden er studies uitgevoerd moeten worden om te onderzoeken hoe lichamelijke activiteit geïnitieerd moet worden en behouden kan blijven. Tenslotte zouden bewegingsinterventies zich moeten richten op specifieke risicogroepen en aangepast worden aan de specifieke behoeften van deze groepen.

DANKWOORD

Zo, dat ei is gelegd. Zie hier het resultaat van een tijd lang broeden. Eindelijk een tastbaar antwoord op de veelgestelde vraag; 'Maar wàt doe je nou precies?'

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CURRICULUM VITAE

Berber Koopmans werd op 18 augustus 1979 geboren in Heerenveen. In 1998 behaalde zij haar diploma voor Voorbereidend Wetenschappelijk Onderwijs aan de Openbare Scholengemeenschap Sevenwolden te Heerenveen. Aansluitend deed zij de opleiding Gezondheidswetenschappen aan de Universiteit Maastricht en behaalde in 2003 haar doctoraaldiploma voor de afstudeerrichting Bewegingswetenschappen. Zij liep stage bij de afdeling Sportgeneeskunde in het Máxima Medisch Centrum te Veldhoven. Hier deed zij een studie naar de effectiviteit van het programma 'Herstel en Balans', een bewegingsprogramma voor kankerpatiënten. Na haar afstuderen participeerde zij als onderzoeker in het zorgvernieuwingsproject 'Chronisch zieken in beweging', een project dat als doel had bewegingsprogramma's te integreren in de bestaande zorg voor zowel patiënten met claudicatio intermittens als patiënten met type 2 diabetes. Vervolgens deed zij haar promotieonderzoek aan de Faculteit Sociale Wetenschappen van de Universiteit van Tilburg. Dit onderzoek vond plaats bij Praktijk-ondersteuning Zuidoost-Brabant (POZOB), waar zij momenteel werkzaam is als wetenschappelijk medewerker bij het Diabeteszorg Zuidoost Brabant (DIAZOB) project, één van de koploperprojecten in het kader van het landelijke Programma Diabetes Ketenzorg.